With the writer's compliments

(12)

I

ATHEROMA.

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ATHEROMA.

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(Plates I. and II.)

The generally accepted view that atheroma is a senile degeneration of the arterial coats, bequeathed in many cases as a legacy to old age by youthful indiscretion, is necessarily both incomplete and unsatisfactory. It is incomplete, in so far as it either overlooks or discredits the many cases of atheroma which occur in the young and the innocent alike. It is unsatisfactory, because it attempts to gloss over our ignorance of the essence of this disease by a term which explains little and implies much. Yet it has been known, on the one hand, for nearly half a century, since Sir James Paget drew attention to the subject, that sclerotic valves were frequently attacked with acute disease, an observation subsequently confirmed and extended by Drs. Goodhart, Osler, and others; on the other, for a somewhat shorter period, through the researches of Professor Virchow, that endocardial and endarterial atheroma were practically identical. My researches into the histology of this protean disease, whether met with in the heart or in the arteries, in an acute or in a chronic form, trend in the same direction, and I feel assured that we shall most truly appreciate the importance of atheroma, as a pathological event, by adopting a comprehensive view of its nature and significance.

The Etiology of Atheroma.

The mesoblastic origin of the blood vascular system, and its early seclusion in embryonic mammalian life, from direct communication with the environment, point to nature exercising a watchful care to prevent the invasion of the blood by foreign particles. There are numberless natural safeguards, partly of epiblastic and partly of hypoblastic descent, whose function it is to prevent so grave a mishap. As long as these safeguards remain structurally sound, they meet the requirement of the case admirably. When, however, from any cause, some of them

become unsound, to just that extent the blood is exposed to contamination. The discovery of various microbes in the sprouting growths of infective endocarditis gives presumptive evidence of the presence of foreign particles within the living blood vessels.[1] In the more chronic forms of atheroma, the existence of these organisms within the vessels is mostly unproven, although the researches of bacteriologists, by yearly adding to the list of diseases due to the presence of microbes in the vascular system,[2] make it clear that few adults can hope to have escaped one or many successful invasions of their blood by these living particles alone. It is, therefore, by no means improbable that advanced atheroma, when found, will have a clinical history pointing to some previous blood contamination by minute intruders. This topic will next demand a few words.

Throughout life the physiological relationship of the hypoblast and the mesoblast is very close, much closer indeed than is that probably existing between the descendants of the epiblast and the latter. In the adult, for instance, the dependence of the body, as a receptive machine, upon the functional soundness of the mucous membrane and its glands is well known. We daily absorb and assimilate many ounces of nutriment. Much of this finds its way into the blood. In health, glandular and other devices, doubtless, render this constant influx of extraneous material for the most part aseptic and so far innocuous. The pulmonary vesicles, again, bring the environment and its minute inhabitants into still closer contact with the blood than even the mucous lining of the alimentary canal does, and yet no evil necessarily results. When however, by disease or injury, an unguarded communication has been established between the blood vessels and the outer world, this aseptic condition of the blood may at any time cease, and indications of atheroma of the vascular walls may appear. In all these cases the epithelium undoubtedly is the chief safeguard against the intrusion of foreign particles into the blood current. In health the epithelial lining of the hypoblast is probably shed frequently, and along with its scales any adherent particles are also removed. This physiological operation usually answers well. When, however, an accumulation of extraneous particles has occurred in some mucous fold or recess, whence removal is

[1] Winge, of Christiania, in the year 1869, appears to have been the first to suggest the presence of micro-organisms in the blood, as a cause of disease.

[2] I may here enumerate a few of the micro-organisms discovered in the blood by different observers. Pollender described the occurrence of *Bacillus anthracis* in the blood of persons suffering from wool-sorters' disease. It is usually associated with some leucocytosis. Obermeyer, in 1874, first drew attention to the presence of a spirillum in relapsing fever. It is found in the blood only during the paroxysms of the disease. Tubercle bacilli (Meisels), *B. typhosus* (Rütimeyer), bacillus of glanders (Löffler), *B. hydrophobiæ* (Bareggi), *Plasmodium malariæ* (Marchiafava), and several varieties of streptococci (excluding animal parasites, such as distomata, filariæ, etc., which are scarcely micro-organisms), are all of them occasional occupants of the blood vessels. Many others have been noted as occurring in the blood by various observers, but their investigations for the most part require confirmation.

difficult or tedious, these scales of shed epithelium may rest awhile with the other particles, and together with them form a source of irritation to the adjacent tissues, leading to the rapid production of successive layers of mucous scales. If the block is not serious, this cell proliferation is doubtless sufficient to re-establish the functional soundness of the membrane. It may often happen, however, that the rapid cell formation may increase the mischief which it in some cases can avert. And when the intruding particles are living, and capable of spontaneous increase, this failure must be the rule. When, moreover, the intruders are endowed with movement, and are actively hostile to the host, his misfortune is their opportunity. If sufficiently minute they may pass through the so-called cement substance beween the epithelial scales into the tissues beyond,[1] or they may find their way there through the denuded basement membrane. The horny epithelial layer, as far as my experience serves me, is rarely penetrated by microbes, so long as it is sound; the epithelial-loving parasites, as described by Foà, Ruffer, and others, may be exceptional. Furthermore, the intruding particles occasionally consist of finely divided inorganic matter. If the observations of C. Isnard on the causation of arterio-sclerosis are confirmed, we shall find such a substance in lead and its salts, many of which are insoluble. Having in some manner eventually effected an entrance into the mesoblastic tissues, and hence by accident or design into the blood, I shall for awhile leave the intruding particles in order to investigate the clinical histories of the cases appended in the table.

Statistics to be of value in atheroma ought to be both voluminous and exhaustive. I cannot hope that the tabulated cases will settle conclusively the etiology, or indeed any other point in the history of this widely distributed disease. My reason for here giving them is that, with two or three exceptions, they represent cases which have come under my own observation. I shall, however, draw attention to a few significant facts, which a perusal of the table elicits. First, there is an exceptional preponderance of males over females in those affected by the disease. There is, again, a considerable number of cases in which a history of one or more attacks of arthritic rheumatism was obtained. This coincides with Isnard's observation. Tubercular disease, with associated pulmonary or intestinal lesions, accounts for several deaths. Malignant disease, including a case of lymphadenoma, is noted in 6 patients. In two of these cases, however, the aorta was converted for a great portion of its length into a rigid calcareous tube, a condition unrecorded in the other tabulated cases. Syphilis is mentioned in three cases only, in one of which it was widely spread. A history of this disease is often very difficult to elicit from a patient. After giving due weight to this circumstance, I still think it doubtful whether

[1] Some writers deny the existence of "cement substance." Heidenhain has attributed considerable mobility to the hyaline adherent borders of the cells lining the small intestine in vertebrates; Hardy and M'Dougall in daphnia; Greenwood in lumbricus.

syphilis exercises any unusual influence in the production of atheroma. If we classify the lesions of the alimentary tract associated with atheroma in the table, we shall find seven cases of ulceration of the stomach, small intestine, and appendix. In two other cases impacted gall-stones are noted. Large abscesses were found in three other patients. The lungs were involved in many cases; the kidneys in a still larger number. I shall return to this subject at a future period. In some cases clinical history points with no uncertain indications to a flaw in the hypoblastic tissues as the portal for the admission of noxious particles into the mesoblast; in many others, for various reasons, it fails to give this evidence.

The earliest age at which I have found distinct indications of atheroma was in the aorta of a girl of $2\frac{1}{2}$ years. In the table there are 12 persons, who were under the age of 26 years at the time of death. These numbers give a percentage of 23 on the cases here tabulated.

The tabulated cases were, with few exceptions, obtained from the *medical* wards of a hospital. Owing to this fact, flaws of the integument due to accident or injury (with one exception, where death was due to a severe burn) are excluded from them. The mammalian integument with its associated glands and horny epidermis, when these exist, constitutes a great defensive and excretory system, by protecting the blood vessels, on the one hand, from unseen intruders, and by assisting, on the other, the kidneys and other excretory organs to remove effete material from the circulation. In performing these functions, it is seldom necessary for the skin to assume the rôle of an absorbent system also; and consequently blood contamination through these channels is probably rare. When, however, as the result of accident or injury to the epidermis, a direct communication is established between the mesoblastic tissues and their environment, the introduction of foreign particles into the blood is only a work of time.

The Development of Atheroma.

Although atheroma is pathologically a general disease, inasmuch as it may occur at different and distant points of the vascular system simultaneously, or within a short interval of time, yet as regards its morbid anatomy it is distinctly a local disorder. Each atheromatous patch has an individual history attached to it, which includes its development, its growth, and, in some instances, perhaps, its decay.[1] The patches, again, have this peculiarity; they may grow independently, for they are often found at different stages of growth in the same vessel. Apparently, too, atheroma may spread either by peripheral

[1] As regards the time required for the development of an atheromatous patch, little is known. I have found elevated patches of milky atheroma in the aorta of a boy, aged 11, after a fortnight's illness from appendicitis; in that of a girl, aged 17, after an attack of pneumonia lasting the same period; and in that of a girl, aged 18, 10 days after a severe burn.

extension from a single centre, or it may be due to the coalescence of several diseased foci. In its development and growth, atheroma has a remarkable predilection for certain vascular sites. In a majority of cases this selective tendency of the disease is readily followed, although after severe and protracted illness the extent and variety of the morbid changes may render the process difficult. I now propose to enumerate, so far as my observations will permit this course, the chief localities atheroma affects in its development and early growth.

Possibly atheroma springs most frequently from the endothelium at the commencement of the aorta. If we take the vascular ring, including the aortic cusps, the sinuses of Valsalva, the orifices of the coronary arteries, and about 2 inches of the surface of the vessel beyond the attachment of the valve, we shall retain the chief structures commonly affected with this disease in its various phases. The mitral valve and its appendages, the chordæ tendineæ, are also very frequently attacked, especially with soft fringe-like growths. The endocardium, the pulmonary and tricuspid valves, the remainder of the aorta (especially the upper part of the great sinus), the lesser curvature of the arch, the bifurcation, and the orifices of the large branches, the circle of Willis, and the renal arterioles are more or less often the seat of the disease. Probably no portion of the vascular system is exempt from the ravages of atheroma.

There are certain structural peculiarities of the sites in the aorta and elsewhere most commonly affected by atheroma. My experience is that the aortic sinuses of Valsalva are of all structures the oftenest attacked; and of them the ridge bounding the upper edge of each appears to be *par excellence* the starting-point of atheroma. In this locality, also, the sigmoid lines of attachment of the cusps to the aorta are frequently affected; as are the points of attachment of adjacent cusps, especially that of the attachment of the anterior and the left posterior, and of the two posterior aortic cusps. These remarks apply in a modified degree to the pulmonary Valsalvan sinuses when they are attacked. Upon the semilunar valves themselves, a spot just below a corpus arantii, and thence along a line bordering the lunule on either side, is a favourite situation for atheromatous thickening to commence. The ventricular aspect of the mitral curtains, especially near the points of insertion of the chordæ tendineæ, and the "lines of contact,"[1] just within the free edges of the mitral flaps, are other common sites.

There are some minor peculiarities of structure in the aorta and elsewhere, which seem to influence the deposition of atheroma, and therefore require a passing notice. At the point of attachment of the right posterior aortic cusp in front there arises a broad band of elastic fibres, which, passing upwards along the greater curvature of the arch, originates a series of smaller fibres. These, spreading outwards like the branches of a weeping willow, sweep in bold outlines to the under

[1] To quote the words of the late Dr. Sibson.

surface of the arch, where they meet another band of fibres on the floor of the vessel. The transverse and longitudinal ridges, so formed in the intima of this portion of the aorta, are the favourite situations for atheromatous depôts. Again, if the endothelium of an artery is examined closely, it will be found to be scored by numberless fine lines, each representing a depression in the arterial intima, and functionally no doubt corresponding to a "line of least resistance" on the skin of our palms and soles. Atheroma mostly commences upon and follows awhile the little ridges of endothelium between these lines.[1] On the boundary ridge of the sinuses of Valsalva, for example, these lines are mostly at right angles to the ridge, and atheroma appears in the first instance as a series of whitish striæ on a creamy background. (Plate I. Fig. 10 shows to some extent this peculiarity of growth.) Finally, I shall draw attention to the variety of atheromatous growth, frequently observed upon the valve of the heart, very rarely elsewhere. I refer to sprouting growths. These excrescences are, to a great extent, confined to the ventricular aspect of the aortic valve and to the auricular surface of the mitral. At all events these two sites are most usually attacked. Some pathologists consider that the localisation of these vegetations is in great part determined by pressure and tension. This explanation, although plausible, is in many respects unsatisfactory. For we can with difficulty imagine that the tensile stress—to use a phrase well-known to engineers—of a small spot on a sigmoid cusp, or at "the line of contact" of a mitral curtain, differs greatly from that of the adjacent endocardium, which is rarely affected in this manner. In considering the development of the milky plashes of atheroma, found so frequently in the aorta, I have drawn attention to some structural peculiarities which appear to influence the early deposition of this disease upon the endarterium. This structural susceptibility of certain parts of the vascular apparatus to the reception of a virus is, I believe, the chief determining factor in cases of sprouting valvular growths. The late Dr. Sibson pointed to the border of small bead-like cells just within the edge of the flap, as the seat of early vegetative growth in the mitral valve. My own observations upon the aortic valvular growths lead me to expect the primary atheromatous depôt in a majority of cases on the arterial surface of the cusp between the fibrous ridges below the corpus arantii, whence the disease spreads inwards to the endocardium. This subject will, however, be dealt with more fully at another time. Some sigmoid cusps have a loose fold of endocardium at the edge of the lunule as it passes into the corpus arantii. This flap, when it exists, is often the seat of atheromatous changes. (Plate I. Fig. 3 shows this fibrous flap upon an aortic cusp. Plate II. Fig 7 is a section through a commencing growth on the cusp of a girl of 8.)

In the preceding pages I have drawn attention to the development

[1] The analogy between the development of atheroma and that of xanthoma (especially when the latter affects the flexures of the joints) is marked.

of atheroma, preferably in certain vascular sites, and to certain structural peculiarities in connection therewith. If this statement of the case is haply the correct one, it may be advisable to inquire how these structural peculiarities react on the blood as it circulates past them, and whether the development of the disease can at any time be ascribed to these causes.

A review of the sites commonly affected by atheroma will show that the favourite localities for outbreaks of this disease are conspicuous for some structural irregularities not generally observable. As an illustration of my meaning, I shall mention the frequency with which the great aortic sinuses are attacked, on the one hand; and, on the other, the bosses and ridges upon the cardiac valves and elsewhere. To take an example, the position of a Valsalvan sinus in its relations to the blood stream is unlike that of any other structure of the body. It is distended at each diastole by a backward thrust of the column of blood in the aorta, or in the pulmonary artery, as the case may be, on the closure of the sigmoid flaps. During the cardiac systole, on the other hand, the pocket is shut off from the blood stream.[1] The surface must, therefore, be alternately swept by tumultuous eddies, as the blood closes the semilunar valves, or bathed in a layer of comparatively quiescent blood. Let me next take the case of a corpus arantii at the aortic orifice. Here we have a distinct obstruction to the blood current, just where the bed is narrowest and the stream is consequently fastest. Atheroma, in my experience, most usually attacks that part of the cusp (in the closed valve), immediately external to the projecting body (Plate I. Figs. 1–4). Now it is exactly at this spot that we might rightly expect a blood eddy once during each cardiac cycle. Again, there are certain portions of the arterial system, where dragging or pulling stresses must modify locally the effects of the circulation upon its elastic walls. I allude especially to the lines of attachment of the semilunar valves, and to the orifices of the smaller arteries; localities often affected with atheroma.[2]

We are so accustomed to consider the blood as a liquid physiological unity, containing in health a definite percentage of semi-solid material, intimately commingled within it, that we too often overlook the wonderful precision with which the relative proportions of these constituents remain practically constant, and the means whereby this end is accomplished. Among the physical processes for ensuring the intimate admixture of the corpuscular elements with the blood plasma doubtless the numerous intravascular eddies and back-currents play their part. However this may be, we find "a little over five millions of corpuscles

[1] According to Brücke, the sigmoid flaps are closely applied to the arterial walls during cardiac systole; Ceradini and others maintain that they float in an intermediate position. It matters not as regards the present contention which of these views we accept. Probably both are partially correct; Brücke explains what happens at the beginning of the systole, Ceradini the position of the valves subsequently.

[2] Mr. Holmes says: "The aorta, popliteal, and axillary artery seem most liable to disease as being most constantly subject to stretching, and the latter to forcible rupture."

in each cubic millimetre" of our blood, and that these bodies are in the proportion of "one white corpuscle to 600–1200 red ones." Doubtless the endless physiological attributes of the blood are in great part due to the constant numerical relationship that exists between its chief component factors.

I have already pointed out some of the bye-paths, whereby foreign adventitious particles can gain access to the circulation. I shall now endeavour to follow these intruding particles in their wanderings through the blood vessels. When foreign particles find their way into the blood, as, for instance, *Streptococcus pyogenes*, there is no evidence to show that they are at any time distributed through the plasma with a uniformity comparable to that observed by its proper corpuscles. Indeed, pathology points to their dissemination by the blood in scattered groups, a mode of dispersal which accounts, it may be, for the simultaneous appearance, as in the example cited below, of multiple abscesses in distant parts of the vascular system, but which is far removed from simulating the intimate admixture of fluid and solid elements which exist in the blood itself. (Cf. Case 50 of Table.) From what is known of the behaviour of viscous fluids we may assume that the density, the size, and possibly the surface tension of these semi-solid suspended corpuscles are concerned with other conditions in producing the homogeneity of the admixture called blood. The chances, then, of any foreign particles fulfilling the physical conditions necessary to their uniform dispersal through the plasma are extremely small, and we may reasonably refuse to accept them.

Owing to anatomical details I need not recapitulate, the group of intruding particles generally enters the blood vessels by one of the arterioles, capillaries, or venules in the periphery. The chief exception to this course is in the case of intruders directly entering the great central veins by way of the thoracic duct. In the other cases the living microbes or other minute particles quickly find themselves within the veins and hurried along by the steady "viscous flow" of the blood in those vessels. From what is known of the behaviour of viscous fluids in slow motion, notably from Mr. Trouton's clever experiments, we may assume that they are borne past the many valves met with *en route*, without encountering the swirls and whirls to be expected in streams of less viscosity. Neither is there any pretext for hindrance or delay, until the heart is reached. When, however, this organ is invaded, the physical conditions of the environment of the particles are changed. Instead of the quiet viscous flow, hitherto encountered by them, their path is beset by throbbing waves and rapid whirls. Caught in these turbulent vortices, like flotsam in the swirling backwater of a freshet, they are buffeted around, until an ebbing reflux strands them away from the turmoil, in some quiet recess. What becomes of them subsequently I shall consider in a future page. Owing to the distensibility of the pulmonary artery, as shown by Lichtheim, Waller, and others, and to the

thinner muscular walls of the right ventricle as compared with the left, the blood stream at the pulmonary orifice may more closely resemble in its physical conditions the quiet viscous flow of venous blood than the turbulent current at the aortic opening. At all events, many foreign particles appear to evade without difficulty the eddies of this pulmonary Scylla, although they subsequently become entangled in the whirls of the aortic Charybdis.

When incipient atheroma has attacked the aorta, the lesion frequently assumes the semblance of sinuous elevated ridges on the endothelium. These lines or ridges vary in degree of curvature from the annular or spiral form to a slightly undulating streak on the inner surface of the vessel. In some cases the pallid ridges interlace with one another, and form a delicate tracery just above the aortic valve (Plate I. Fig. 9). It is difficult to account for the rings and spirals of atheromatous growths so commonly seen in this situation. If, however, we remember the spiral eddies, which agitate the blood stream at the aortic orifice, may we not consider the close association of liquid vortices with atheromatous tracery in these cases to be more than a fortuitous coincidence? may we not have in the former an important factor in the causation of the spiral ridges?

The Growth of Atheroma.

The fibrous investment—the "inner longitudinal fibrous tissue" of Remak—immediately outside the aortic endothelium, forms, I believe, the basement of a connective tissue network, which binds the various components of the arterial walls together. The basement membrane sends fibrillar strands obliquely outwards at intervals, whence delicate trabeculæ are given off—(1) to ramify amongst the meshes—the "fenestræ" of Henle—of the longitudinal elastic layer of the intima, and outside of this to form (2) a loose areolar bed. This bed separates the inner from the middle coat of an artery, and permits free movement between them. Subsequently the network surrounds the components of the middle coat, and ultimately becomes the loose fibrous investment, named the adventitia. During life the meshes of this network are bathed in blood plasma, which is however shut off from the circulation by the endothelium and basement membrane above described. Even during health this plasma may contain a few scattered corpuscles, which are stained by logwood, and basic aniline dyes. If a section is made through an atheromatous plash in the aorta the above structural details can be generally made out, but in addition thereto the endothelium and basement membrane are seen to be invaded by many corpuscles, which stain readily with basic dyes, as did the others. When the disease is in a very early stage these corpuscles are not numerous elsewhere. If the atheroma is more advanced, the corpuscular invasion will have extended outwards through the basement membrane to the tissues beyond,

apparently following, in the first instance, the strands of connective tissue in their oblique passage among the fibro-elastic bundles of the inner and middle coats. Meanwhile the spaces among the fibres, and even the fibrous bundles themselves, will be found to be occupied by members of the invading horde. The former, especially where the tissues are loosely netted, as around the outer surface of the intima, become opened up and enlarged; the latter are split up, more or less completely, into their ultimate fibrils.

The nutrition of the arterial walls is doubtless mainly dependent on the blood plasma, which permeates their interstices. In a healthy vessel the contractility of the media, and the longitudinal plication of the intima at each arterial systole, empty more or less completely this canalicular system, and so ensure the frequent renewal of its contents. When dilatation of these cavities occurs, especially if it is accompanied by changes in the elastic lamellæ, and by thickening of the fibrous network, as in early atheroma, the resiliency of the affected tissues must be seriously interfered with, and their nutrition impaired. One of the earliest tissues to feel the secondary effects of malnutrition is the endothelium. The arterial lining membrane at the affected spot undergoes so-called "fatty degeneration," which is never a primary affection in my experience, and in this opinion I am supported by the authority of several eminent pathologists, both at home and abroad: notably by the late Dr. Moxon, and, more recently, by Mr. Timothy Holmes. According to my view fatty degeneration of the endothelium is always preceded by, and associated with a corpuscular invasion, as above described.[1] Occasionally there is hyperplasia of the endothelial cells. In either case the intima is quickly denuded of its inner lining, and the basement membrane is exposed to the blood stream. Another effect of these intermural changes, the result of atheroma, and a purely local one, is a stagnation of the blood plasma within the dilated tissue meshes, especially those in the intima itself, and in the connective tissue between that and the middle coat. This stagnation of the plasma is closely associated with the thickening and stiffening of the inner coat, mainly by a fresh growth of connective tissue. If the wall of an artery is examined at this stage of the disease, the folds and wrinkles of its lining membrane, to which I have elsewhere called attention, are no longer visible, and in their place is a smooth projecting patch of white unyielding tissue. This patch represents the inner layers of the intima, which have lost their pliancy through structural changes, such as those described above. On section we shall find the outer laminæ of the intima honeycombed with small holes, in some of which are to be seen one or more corpuscles. At intervals appear cavities containing several corpuscles and fibrillar débris. Sooner or later the walls of

[1] Mr. T. Holmes considers that the "fatty changes in the arteries are preceded by an increased cell-production characteristic of inflammation."—*System of Surgery*, 3rd edition, vol. ii. p. 15.

these cavities, and any projecting fibrils within them, become coated with a granular deposit, consisting of earthy salts;[1] subsequently the granules give way to globular and boss-like projections, until the whole bed of the intima at the diseased part is transformed to a thin bony plate, having on its inner surface, it may be, oblique calcified lamellæ, which pass inward as far as the basement membrane. The latter is usually stretched tightly over the petrified intima, as a fibrous covering; occasionally this fibrous membrane splits and allows a calcareous boss to invade the lumen of the vessel itself. Rarely the basement membrane is converted into a calcified plate, which is extremely thin and brittle. If the corpuscular elements in the affected parts are numerous, the basement membrane, or its representative, rapidly disappears, and the atheromatous ulcer arises. The base of the ulcer is usually the petrified bed of the intima. When an inelastic atheromatous plaque forms a part of the coats of an artery, the vessel frequently becomes dilated at the part. Aneurismal pouches are an occasional although, in my experience, a rare termination of atheroma.

I shall now briefly describe certain modifications of atheromatous growth, only observed upon the cardiac valves. In cases of aortic atheroma the cardiac valves and the endocardium, as is well known, are often affected with the white plashes of the disease. The arterial surface of the semilunar valves and the ventricular surface of the mitral are usually attacked in the first instance. If a section of a diseased valve is examined, it will be found to be the seat of a corpuscular invasion. This invasion is associated with a widening of existing fibrous meshes, a new connective tissue growth between the elastic bundles, a splitting up of the latter into their ultimate fibrils, and a consequent loss of pliancy. In other words, subsequent changes in these regions are similar to those observable in atheroma of the arterial walls. Occasionally, however, the disease attacks the line of attachment of a cusp within the Valsalvan sinus. In this case there is a silting up,[2] so to speak, of the bed of the sinus (see Plate I. Fig. 8), with a contraction of the arterial orifice. On section, wedge-shaped masses of new tissue are found just beneath the floor of the Valsalvan recess. These are composed of corpuscular elements such as those before mentioned, new connective tissue fibres, and many cavities and small holes, within which are visible one or more corpuscles. The new tissues push apart and invade the proper structures of the sinus. In all this we find only an extension of that atheromatous process we have observed in the arterial walls. The subsequent petrifaction of a similar growth, by a process analogous to that already described, as occasionally taking place in the arterial walls, confirms my

[1] Mr. Rainey, I believe, first drew attention in 1857 to the effect of colloid solutions on crystalline forms, by inducing "molecular coalescence" in the latter. Drs. Guthrie and Ord have also worked at the subject.

[2] It is possible, as my friend Dr. Adolphus Richardson has suggested, that the systolic murmur heard over the commencement of the aorta in atheromatous disease may occasionally be due to this cause (see Guttmann, *Bibliogr.*).

opinion that they are practically identical. The slight differences observable in the two structures, *e.g.* the greater size of the osseous cavities, and the petrifaction of the whole thickness of the cusp, are mainly due to the anatomical peculiarities of this organ, and not to any essential difference in the manner of osseous deposition. When the ventricular surface of the aortic valve is affected in or near a corpus arantii, either primarily (see p. 6), or as an extension of the disease from the arterial surface, so long as the pliancy of the valve at the line of contact with the aorta is not impaired, we may expect to find a sprouting, warty growth, or vegetation. I shall first consider the case, where the ventricular growth is secondary to atheroma of the arterial surface, and I shall refer to a specimen, which exemplified on the three cusps three successive stages of the process I describe (Plate I. Figs. 1, 4). One aortic cusp of this patient (Case 29 of the Table), just below a corpus arantii was decorated with a single pendulous growth. On section this proved to be a single-celled cavity, having for its walls a continuation of the fibro-elastic layers on that aspect of the cusp (Plate I. Fig. 4). The cavity contained a pale straw-coloured material, which, for reasons I shall give on another page, I imagine to have been of a jelly-like consistence during life. In the cusp there were the usual signs of somewhat advanced atheromatous growth, just before petrifaction commences. The central parts of the curtain were separated by many interfibrillar cavities in the usual manner, and, I conjecture, the cell within the fibrous pendant was similar in its nature to the cavities. On the second cusp, in a like position, there was a tough warty elevation, at the lower edge of which grew a fibrous flap. The flap in the fresh state could be so adjusted as to cover accurately the projecting part, and the whole then formed a pendant resembling that upon the other cusp. The superficial ventricular layers of the cusp passed into and formed the skin-like flap, which at first must have covered the young sprouts, until their vigorous growth so far stretched their capsule as to produce its atrophy locally. The suction of the left ventricle, to which Dr. Dickinson has recently called attention, effected the final detachment of the flap from its bearings. The third cusp had a somewhat similar rough fibrous vegetation to that just described, but it was without a flap, and its bosses were tipped with soft thready fibrine.

The suction of the auriculo-ventricular cavities during a cardiac diastole tends to produce many special modifications of atheromatous growth on a cardiac valve. The well-established fact that sprouting growths are mostly found on the ventricular surface of the aortic valve, and on the auricular surface of the mitral, points to some physical cause in operation on one side of the valves, which is not obtainable on the other. I must here remind my reader that this remark applies to the growth of an atheroma, and not to its development, which has been discussed previously. In my experience these vigorous sprouting growths, whether they occur on one or the other set of valves, may be

structurally divided into a soft fungating cortical substance, and a central core of fibro-elastic tissue, which passes directly into the proper tissues of the cusp. This latter portion of the growth has the ordinary structure of atheroma, and except for the somewhat larger size of its cavities possibly, and for the greater number of its corpuscles, there would be some difficulty in distinguishing this lesion microscopically from an atheroma of the arterial intima. Out of the central core one or more branches usually pass for some distance into and support the fringe; these branches are also composed of fibrils, which retain in their midst a swarm of well-defined corpuscles, similar to those above mentioned. When, however, the peripheral branches are ultimately reached, the fibrillar structure disappears, and a homogeneous or coarsely granular material takes its place; into this tissue the van of the corpuscular swarm can be traced for a short distance; the corpuscles, then, gradually lose their deeply-stained contour, become somewhat swollen and granular, and eventually disappear, each leaving a slight macula, to mark the spot of its dissolution.

Caught in the swirls of arterial blood, we left the intruding particles for a while (p. 8). I shall now continue their history. I have already drawn attention to the importance of the epithelial lining, as a safeguard against the introduction of foreign particles into the blood; indeed, I imagine the endothelium of the arterial system to be only second to the epithelium, in its power to withstand the assaults of foreign elements, whether they be living or not, provided the attacks are directed against its inner surface. At all events, I have not found microbes within the healthy endothelial cell, although I have repeatedly looked for them there. When, therefore, the intruding particles, much to their discomfort possibly, first find themselves hurried along by the blood stream, they are not in a condition to actively injure the vessels, through which they may pass, even though each one possessed the dozen flagella ascribed by some observers to a typhoid bacillus. Let us, however, assume that a group of noxious bacteria have successfully established themselves in one of the numerous fibrous plications within an aortic Valsalvan sinus. "Cabined, cribbed, confined," within a narrow space, I know not whether these organisms would contrive to thrive and multiply; but I believe that any attempts on their part to force a passage for themselves through the endothelium would be unavailing, so long as that membrane was locally intact. In a majority of cases, doubtless, foreign particles, when conveyed by the blood to some quiet recess away from its eddies, are merely passive agents, and their movements are guided entirely by circumambient currents throughout their intervascular existence. If, then, from any cause, these currents are unavailable, their locomotion at once ceases, yet this event must be a rare one even in a blood vascular recess.

The oft-quoted researches of Metchnikoff upon this subject, confirmed as they subsequently have been by many distinguished

histologists both at home and abroad, need not detain us long in the present instance. The foreign particles, whatever their nature may be, are certainly a superfluous, if not an inimical addition to the blood, and as such ought to be removed thence as soon as may be. For this service nature has detailed certain corpuscles to act as blood scavengers. To these bodies a small group of blood invading particles, which circumstances have either rendered stationary, or endowed with restricted movements, will fall an easy prey. On occasions, as we shall subsequently learn, it may be otherwise.

In the description of the histological peculiarities of atheroma, reference was frequently made to corpuscular swarms, which permeated the affected tissues. I propose now to give fuller details of these minute bodies. Ehrlich pointed out about fifteen years ago that the colourless blood corpuscles, or rather the granules within them, exercised a selective power in relation to aniline dyes. He also showed that in the normal connective tissue the cellular elements found in the network were stained deeply by basic aniline dyes, distinguishing them from many leucocytes (those of the newt excepted). I believe that in a diseased state he admitted the existence of occasional "basophile" leucocytes in the blood of man. However this may be, my own opinion, based on some years' experience, is that in atheroma these "mastzellen" or "nuclear bodies," as I prefer to call them, are blood-born corpuscles, despite their aniline reaction.

Nuclear bodies are small masses of protoplasm, about the size of ordinary leucocytes. Their size is, however, somewhat variable. In fluids (*e.g.* blood plasma) they may assume a spheroidal shape, but within the arterial walls the usual shape affected by them is pip-like or "nuclear." Hence their variable contour, when seen *in situ* under a microscope. In common with their congeners, the ordinary leucocytes, these bodies possess during life the means of individual locomotion by pseudopodial protrusion. Under certain conditions, to be considered hereafter, their activity is apparently increased, and they may appear as minute worm-like bodies. In all cases, when embedded within the tissues, they can be deeply stained by logwood, and basic aniline dyes. Under a high power they are then seen to consist of a lightly-stained plasma, containing deeply-stained granules within.[1] Nuclear bodies are also stained by watery solutions of eosin, but the reaction is due in this case, as in others pointed out by Delépine, to the staining of the plasma instead of the granules. It is, therefore, not a differential stain. Carmine also stains these corpuscles. The most satisfactory stains in

[1] If the distinction, based upon the reaction of certain cell-granules with methylene-blue, is a reliable one, Mr. W. B. Hardy has happened on a differential stain of value in discriminating between "basophile" corpuscles. In astacus he found the cells with rose-staining granules lodged in the spaces of a peculiar tissue which forms an adventitia to some of the arteries. In vertebrates they occur to a marked extent in the peculiar adventitia of the blood vessels of the spleen. He regards it as probable that the blue-staining granules are absent from wandering cells.

my hands are a basic aniline solution of Bismarck-brown and Martindale's hæmatoxylin solution (Ehrlich).

The removal of a small group of foreign particles from the blood by leucocytes is probably effected with speed and efficiency. Yet the primitive method adopted by these minute organisms of swallowing their obnoxious visitors is undoubtedly open to serious objections from a sanitary standpoint, whenever large numbers are dealt with. Nuclear corpuscles, as met with in atheroma, are, I take it, essentially blood scavengers which have done their work.

The phylogeny of the vascular system in vertebrates has been studied by Bütschli, Ziegler, Hubrecht, and others. Bütschli conjectured that the blood cavity of vertebrates was derived from the segmentation cavity. Ziegler pointed out that the blood and lymph vessels of vertebrates together represent morphologically the primary body cavity in nematodes. The pleuro-peritoneal cavities, on the other hand, have nothing to do morphologically with the primary body cavity. They are formed separately, and are only secondarily connected with the vascular system. The blood vascular system, again, is descended morphologically from the hæmolymphatic system of some invertebrates —arthropods, for instance. It is archicœlomic in its nature. Vertebrate lymph, inasmuch as it is an albuminous fluid containing leucocytes, is more nearly allied to the hæmolymph of many invertebrates than is blood. I conjecture, however, that in the interspaces of an arterial wall, when filled with plasma, we have a close resemblance to the hæmolymph canals which permeate the tissues of arthropods and other invertebrates.

Before continuing the life-history of a nuclear corpuscle, it will be useful to ascertain, as far as may be, by glancing over the animal kingdom, how the blood is cleansed and freed from noxious and effete material in some of the lower classes. Mr. H. E. Durham has described how the amœboid corpuscles of a star-fish, *Asterias rubens*, after devouring some substance which it is to the advantage of the organism to excrete, work their way out through the body wall. In *Asteroidea* there are no nephridia. In *Clepsine* and *Nephelis*, where they are present, Mr. Shipley states that the nephridial funnels connect the vascular system directly with the body cavity. He confirms Bourne's observations on this point. He has found the nephridial sacs to contain numerous corpuscles from the blood. These amœboid corpuscles "seem to be degenerating, in some cases they appear rather more granular than the normal corpuscles of the blood." It has occurred to him that we have here to do with a similar phenomenon to that observed by Durham; only in this case the blood corpuscles, instead of working their way to the exterior after their meal, "are taken up by the open funnel of the nephridium, and in the sac they disintegrate and are eventually thrown out from the body." In *Hirudinea* and in *Nemertea* the nephridial system, although it is not in all cases in direct

communication with the vascular system, is very closely connected with the blood spaces by its inner ends, which frequently lie within them. Finally, in the vertebrate *Bdellostoma forsteri*, Weldon has found a number of fine tubes anastomosing and running through the substance of the head kidney. These tubules open, on the one hand, into the pericardium, and on the other into a central duct. In this duct was a blood clot similar to those in the blood vessels. We find, then, among the lower animals, at all events, the blood to have very close relations with the nephridia, and that there is good reason for considering one of the functions of these organs to be the removal of disintegrating corpuscles from the blood.

I have already stated my opinion that the nuclear bodies, seen in the atheromatous walls of the artery, are vagrant corpuscles from the blood. It will be expedient to give here, in detail, the grounds for this statement. First, in their relationship to the endarterium, nuclear bodies are most numerous on the inmost layers of an arterial wall, when atheroma is commencing. At this stage of the disease it is by no means unusual to find one or more corpuscles protruding into the lumen of the vessel—corpuscles which, in appearance and in physical properties, are, as far as I can judge, identically the same as those visible in the tissues adjoining. Secondly, these bodies react to stains in a similar manner. Thirdly, in size they closely approximate that of a leucocyte. Other characters, common to the two corpuscular forms, might possibly be mentioned in support of my contention, but space will not allow of their recital. If we admit the nuclear bodies to be the blood scavengers, and to perform their functions by devouring any foreign or effete material within the blood vessels, it follows necessarily that after their objectionable meal they should remove themselves and their ingesta out of the blood as soon as may be. In the lowest forms of life supplied with blood we have seen that the amœboid corpuscles, whose functions in the economy of the star-fish are closely similar to those of the nuclear bodies in our blood, promptly betake themselves to the outer world through the body walls of asterias, so soon as they have fulfilled their mission as scavengers. By this action they undoubtedly remove, in a simple and efficient manner, any noxious material they may have met with and swallowed. Let us consider whether we can trace any corresponding anxiety in the surfeited corpuscles of our own blood. The manner in which atheroma is developed will furnish an answer to this query. I have elsewhere stated that the arterial endothelium appears to possess in a modified form the capacity of resisting the attacks of micro-organisms, when directed against its inner surface; a resistant power which cutaneous epithelium has acquired in a high degree. Now, although the endothelium may prevent by this means any ordinary attempts at perforation of the arterial walls by a foreign intruder, or even by a vagrant leucocyte in the casual manner ascribed to its Ulyssean wanderings by some writers, it is powerless to check the exodus of a

devoted horde of these scavenging nuclear bodies in an effort to purify the blood at once and effectively from a dangerous intruder.

If a properly-stained section through an atheromatous plash is examined microscopically, the inner endothelial layer will be seen to be invaded by many deeply-stained nuclear bodies. That they are vagrant bodies and not constant inhabitants of the endothelial cells is rendered more probable, among other reasons, by their unequal distribution over the membrane. In many cases two corpuscles are found to have invaded one cell, or several cells appear without a stained nuclear body. In the endothelium these bodies often assume an ovoid or spheroidal shape, as they appear to do in the blood stream. When, however, the tough basement membrane is reached their true wanderings commence, and they mostly assume shapes, expressive of greater activity, such as the pip-like form before alluded to. By the pointed extremity they push aside the elastic and other fibres, and force a passage amid the fenestræ, widening the spaces and loosening the fibres in their outward course. Their exodus through the intima is mainly regulated, as I have suggested elsewhere, by the oblique direction of the strands of connective tissue, which bind together the various layers of elastic and other elements in the arterial walls.

If the above interpretation of the functions of nuclear bodies, and of the manner in which they are carried out, is the correct one, and, of course, I assume that it is so, it will be interesting to inquire, what becomes of these bodies subsequently. This I now propose to do. In describing the histology of the soft tuftlike growths on a cardiac valve I drew attention to the occurrence of gradual changes in the shape and appearance of the nuclear bodies as they approached and passed into the soft tissues of the fringe (p. 13). These changes were ascribed to the gradual dissolution of the corpuscles in the newly-formed fringe. In the specimen to which the description specially applied (No. 51 of Table) the growth began from an atheromatous patch on the ventricular aspect of the mitral valve. From this point the disease had passed, as it usually does in these cases, through the valvular curtain into the pendulous auricular growth beyond. Whilst the ventricular layers of the curtain were overrun by many deeply-stained nuclear bodies, as our eyes passed in review a section of the fibro-elastic strata of the valve, these bodies became visibly less numerous until, upon the auricular side in the newest growth, they disappeared in the manner stated. Now the above account of the progress of the vagrant corpuscle from its home in the blood to its dissolution in some neighbouring tissues, probably represents what actually takes place to many of them after a poisonous meal. And this is an explanation of the presence of maculæ amongst the fibrous layers of an atheromatous plaque, especially in the middle and outer coats of a vessel.

Forcing its way by a leech-like movement through the soft gelatinous plasma, which fills the interfibrillar spaces of the arterial walls, our

blood-scavenger may leave, as it undoubtedly often does, a hollow flattened burrow behind it, wherever the plasma is sufficiently viscous or the fibrillar bands are sufficiently separated to favour this occurrence. These streak-like burrows are common objects in atheromatous sections. At times, haply, the microtomist's chisel may lay open a burrow lengthwise, when the nuclear corpuscle is seen at one extremity (Plate I, Fig. 13, *b*). Having penetrated in this wise to the adventitia of the vessel, and being well away from the blood, which, let us always remember, it is seeking, to use teleological language, to purify by its migration, either its strength fails, or, what is more probable, a reaction is set up between its surface and the surrounding plasma, and the nuclear corpuscle becomes motionless and enveloped in a capsule (Plate II. Fig. 12). And so we have two endings to these migrant bodies, dissolution and encapsulation.

Before leaving this subject I shall briefly state my views in regard to the transformation of the ordinary leucocyte of the vascular system into a basophile nuclear corpuscle of atheromatous tissue. In a recent paper[1] on the development of the lymphatic glands, Dr. Gulland has given a well-selected résumé of what is at present known regarding the nature of leucocytes. He concludes that, although there are many varieties of these bodies, a leucocyte may pass through them all in the course of its existence; that is, I take it, it may possibly start life as a young wandering eosinophile cell, to end its career as a giant stationary cell of the bone marrow, spleen, or embryonic liver. However this may be, it fails to explain why we find so large a proportion of basophile corpuscles in atheromatous tissues or in new connective tissue generally, although they are rarely found within the adjacent blood vessels. I, therefore, offer the following explanation of the phenomena described in the foregoing pages. I have repeatedly insisted on the importance of the function of the nuclear body in atheroma, namely, to withdraw noxious matter from the blood; and I here again allude to it, as furnishing a rational interpretation of the variable reaction of leucocytes to aniline stains. The young leucocyte, the eosinophile cell of Ehrlich and his school, is, according to Gulland, not a phagocyte, at least that is the meaning I attach to his words.[2] "Microbes are ingested mainly, perhaps, by wandering cells (not eosinophiles), but also by all varieties of the stationary cells." If a nuclear corpuscle, as seen in an atheromatous plash, is a basophile leucocyte, which has made a meal of some noxious blood particles, and has subsequently betaken itself outside the circulatory system, for the purpose and in the manner I have elsewhere mentioned; and if again young leucocytes are for the most part eosinophiles, surely we have good grounds for the assumption that some important change in its constitution may occasionally convert an eosinophile leucocyte into a basophile corpuscle. If the fact of an eosinophile corpuscle having obtained a good round meal—to use homely language—is sufficient to destroy this aniline reaction, and to convert it at once

[1] *Journ. Path. and Bacteriol.*, Edin. and London, 1894, vol. ii. p. 448. [2] *Ibid.* p. 458.

possibly into a neutrophile or a basophile corpuscle, I think we have an important clue towards the solution of this physiological problem, namely, that the granular contents of the leucocyte, on which the staining reaction apparently depends, vary with the ingesta. When these ingesta are microbic in their character, and, as a consequence, stain deeply in most cases with basic aniline dyes, the leucocytes become basophiles. With other ingesta, possibly of a less virulent nature, the eosinophiles are changed to neutrophiles. Here, then, we have a fairly simple explanation of the varieties of leucocytes, as shown in their reactions to aniline stains.

The After-Consequences of Atheroma.

Although some nuclear bodies terminate their wanderings within a short distance of the artery they have perforated, we must look upon this operation on their part as an evidence of reversion to an ancestral type of amœboid action rather than as an example of the perfected method adopted by these bodies in the discharge of their functions as blood scavengers to man. I have elsewhere (see Appendix B) alluded to the relationship which appears to exist between atheroma and kidney disease. The table appended to this paper extends and confirms this view. Of the 52 cases therein collected, no fewer than 35 had definite renal lesions, mostly of fibroid type, and in this estimate some cases of simple congestion, and others in which the condition of the renal organs was not stated, have been included amongst the healthy cases. When every allowance has been made for these and other accidents affecting the result, we shall still have the startling fact that, according to this table, more than half of the cases of confirmed atheroma are affected with kidney disease. In atheroma of the aorta, to take the vessel most commonly affected with the disease, the *vasa vasorum* are apparently attacked by the nuclear bodies at an early date. The tissues about the nutrient arterioles are especially beset with numerous vagrant, deeply-stained corpuscles. Now it seems probable that some of these bodies, whilst they are blindly wandering amid the aortic coats, may haply penetrate and re-enter this artery, to be at once swept away unresistingly by the blood stream.

In reviewing the gradual development of the nephridial funnels among the lower animals, there seemed some ground for the conclusion that the chief function of these organs was to collect and to withdraw from the blood those amœboid corpuscles, which, after performing their mission as scavengers, were about to disintegrate.[1] It may prove interesting to inquire briefly, whether our own kidneys assume these functions also. I shall first consider whether the morbid anatomy of a fibrotic kidney, as we find it associated with atheroma, will throw

[1] In the mammals, probably, the process of disintegration takes place within, and is modified by the spleen under ordinary circumstances.

any light on this inquiry. Upon examining a section of the diseased organ, we shall at once notice the uneven distribution of the fibrotic changes amongst the renal tissues. One of the earliest structures involved is the Malpighian tuft, or, more precisely, the membrane covering the tuft, and forming part of Bowman's capsule. This membrane is, at an early stage of the disease, studded with numerous deeply-stained corpuscles, which are physically identical with the nuclear bodies met with in the arterial walls. Subsequently other vascular changes follow; a few only I shall here instance, namely, thickening of the capsules, with shrinkage of the tufts, and greatly increased thickness of the coats of the renal arterioles. These changes take place coincidently with the scattering of numerous groups of deeply-stained nuclear bodies about the necks of the capsules, and in the renal connective tissue. Many of these bodies are encapsuled in strands of newly-formed fibrous tissue, and are mostly spheroidal in shape; others, again, can be found of the distinctive pip-shape, which my readers will remember probably betokens active individual movements on the part of a nuclear body at the time of death. In these changes of renal structure we see possibly the wreck of an organ which has been functionally overtaxed. If we consider the nephridial funnels to have been the precursors of the kidneys in the higher vertebrates, it is probable that the functions of the two organs are similar; and, as a consequence, that the kidneys are concerned in the removal of nuclear bodies, when the latter have fulfilled their mission as blood scavengers. Under ordinary circumstances these bodies will have undergone disintegration before they are submitted to the renal tissues for removal. When, however, owing to the presence of an excessive number of foreign particles in the blood, a correspondingly large number of surfeited corpuscles are also present, the stress of the removal of the surplusage will largely fall upon the kidneys.[1]

Referring again to the table, column 3, the observer will find that there are no fewer than 28 cases of pleuritic adhesions noted in this column, exclusive of some cases of hydrothorax. Here, then, we have three-fifths of the recorded cases affected with some, mostly old, pleuritic trouble. Associated with these lesions of the pleural cavities there was in some cases a fibroid degeneration of one or more of the pulmonary lobes. Besides these fibrous changes, incidental to the lungs and pleura, others are noted implicating various organs, yet all consisting essentially in an overgrowth of the fibrous connective meshwork which binds the different parts of an organ together. MM. Duplaix and Isnard have at different times drawn attention to this "sclerotic process" in connection with vascular changes, that is, with

[1] Drs. Jacob and Krüger, in their recent experiments on a case of leukæmia, showed that an increase in the nitrogen of the uric acid and nuclein bases of the urine is associated with the increase in the number of leucocytes.

a luxurious growth of areolar tissue around the vessels, especially around the central arteries. From what has been stated of the rôle assumed by the nuclear corpuscle, in the production of the sclerotic changes of atheroma, it seems probable that these bodies in some mysterious way are directly concerned in the production of all such overgrowths of connective tissue.[1] For whether we observe the young tissue strands on the thickened Glisson's capsule, in the interstices of a granular kidney, or amongst the meshes of an atheromatous aorta, we shall find the same basic staining corpuscles everywhere interspersed amid them.

In considering the passage of foreign particles through the blood vessels, I suggested that the transit was mostly performed by coherent groups of these elements, and reasons were given in support of this view (p. 8). If the facts of the case are here correctly stated, it follows that when foreign matter finds an entrance to the vascular system by any portal within the alimentary tract, the particulate group must pass through the capillary network of the lungs before it arrives at the aorta. In many cases this passage, owing to the small size of the group, or to the mobility of its constituent parts, is readily effected. It must, however, occasionally happen that the group becomes impacted in the lungs. Then nuclear bodies at once strive to remove the obstruction. The engorged corpuscles on the cardiac side of the obstruction may or may not subsequently pass along the pulmonary veins to the left heart, those on the far side will have every inducement to penetrate the vessel's walls, a privilege of which they readily avail themselves. And so they eventually find their way into and increase the fibrous stroma of the lungs, producing puckering of the alveolar tissue, or even fibrous adhesions between the pleural surfaces, if their path leads in that direction. It is often a matter of surprise to find, after death, extensive valvular lesions, or atheromatous ulceration of the aorta, without any secondary thrombi, such as we might be led to expect, in the peripheral vessels. I believe in these cases, many interesting examples [2] of which have been from time to time published, the sequel of pathological events may be explained as follows:—The detritus of the vegetative growth or atheromatous plaque, as the case may be, consists in these instances of finely-divided particles. These "orts," when they obstruct a vessel, are entirely devoured within a short period by nuclear bodies. Living nuclear bodies, I contend, never produce thrombi *per se*, their province is to remove them when discovered. When thrombi occur during life there is strong presumptive evidence that the blood vessels have been invaded by foreign particles, which by obstructing the flow of blood in a vessel have induced clotting and the formation of a thrombus. In nuclear bodies, then, we shall find not only the true blood scavengers, and the producers of atheroma, but

[1] Ziegler and Marchand drew attention to this subject in 1891.

[2] See papers by Drs. Church, Moxon, and others (Appendix B).

also the probable originators of fibrous overgrowth, in whatever part of the body it may appear.

Finally, my thanks are due to Drs. W. S. Church and Adolphus J. Richardson for their kindness in perusing the MS. and for several valuable suggestions regarding it. I am also much indebted to *Virchow's Jahresberichte* for the able abstracts of many of the medical papers referred to in this essay.

DESCRIPTION OF PLATES I. AND II.

FIG. 1.—Two of the aortic cusps from Case 29. At the lower part of the right corpus arantii is a tuberculated growth with a fibrous flap attached below. In the fresh state the flap could be adjusted to cover the growth. The case is fully described (p. 12).

FIG. 2.—Fringe-like growth springing from the base of a corpus arantii, and extending along the border of the lunule.

FIG. 3.—Fibrous folds on the ventricular aspect of aortic cusp affected with atheroma (p. 6).

FIG. 4.—Section of the third aortic cusp, with a pendulous growth attached, from Case 29. Fig 1, (*a*) the growth. × 25.

FIGS 5 and 6.—Sections of the atheromatous tissues highly magnified, showing the dissociation of the fibrous elements, and the widening out of the meshes which follow an invasion of nuclear bodies.

FIG. 7.—Section through an aortic cusp, thickened at (*a*) by atheromatous deposit; at (*b*), on the arterial side, is a recess, the seat of commencing atheroma.

FIG. 8.—Section through a diseased Valsalvan sinus. The bed of the sinus is, as it were, silted up by the interposition of wedge-shaped pieces of tissue (*b*), between the cusp (*a*) and the aorta (*c*). Case 45. × about 3.

FIG. 9.—The arterial surface of an aortic cusp attacked with atheroma.

FIG. 10.—A part of the aorta just above a cusp stained slightly by eosin, showing circinate patches of atheroma. Case 46. × 2.

FIG. 11.—Section of the aortic intima showing the passage of nuclear corpuscles obliquely outwards. Ehrlich's hæmatoxylin solution. × about 500.

FIG. 12.—Section of a renal artery, highly magnified, showing a nest of nuclear bodies encapsuled between the layers of the media and the adventitia. × 1350.

FIG. 13.—Nuclear bodies highly magnified, *in situ*. *a*. Nuclear body surrounded by jelly-like plasma, in which fine fibrils of new connective tissue are visible. *b*. Nuclear body at the extremity of a burrow. *c*. Nuclear body in the act of worming its way through the plasma at death. × 1350.

FIG. 14.—Section through the intima of the aorta, showing the oblique fibres trending outwards. *aa*. Endothelium. The fibres pass from the basement membrane (*b'*) towards the right (*b*). From a photograph.

FIG. 15.—Atheroma of aorta with contracted fibrous kidneys.

APPENDIX A.

Table of Cases of Atheroma showing various Diseases with which the chief Organs were concurrently affected.

Sex, Age, etc.	Vascular System.	Lungs, Pleuræ.	Kidneys.	Other Organs, History, Remarks, etc.
No. 1, F., 55, cook.	Aorta somewhat atheromatous.	Left, œdematous; no vomicæ; pleural surface studded with cancerous growths.	Left, mottled; capsule adherent.	Peritoneum, omentum, and mesentery thickened, and infiltrated with like deposits.
No. 2, M., 47, bricklayer.	Atheroma of mitral valve and ascending aorta; aortic cusps perforated by 2 or 3 small punctures along free border.	Right pleura universally adherent; lungs congested and œdematous.	Large, much congested; urine, non-albuminous.	A glioma in left cerebral hemisphere.
No. 3, F., 50.	Vegetations on 2 aortic cusps; thrombi in both pulmonary arteries, adherent to walls and nearly occluding vessels.	Middle lobe of right lung greenish brown in patches; both lungs œdematous.	Capsules adherent; granular; cortex thin, streaky.	Gall-stones, malignant disease of liver and gall-ducts.
No. 4, F., 38.	Thoracic aorta converted into rigid calcareous tube; heart and abdominal aorta healthy.	...	...	Patient died of malignant disease of the liver. (S. C. H. Museum, C. 58.)
No. 5.	One or two cystic bodies on thickened edge of mitral; 2 aortic cusps coherent; abdominal aorta, a calcareous tube; ascending aorta atheromatous and dilated.	Firm pleural adhesions, over right lung; at left apex small vomicæ; a few vascular tumours size of a swan-shot in lower lobe.	Left, converted to fibrous mass, weight, ¾ oz.; right, 7 oz., healthy; both ureters normal size.	Numerous vascular growths in liver, gall-bladder, and beneath peritoneum; a large ragged ulcer occupied cardiac end of stomach.
No. 6, M., 44. plasterer.	Aneurism of ascending aorta involving pericardium; muscular tissue of heart soft, valves healthy.	Right pleura held 50 oz. clear fluid; left pleura obliterated by firm adhesions; right lung collapsed.	Capsules firmly adherent; finely granular surface.	Liver firm, congested; weight, 3 lb. 1 oz.
No. 7, F.	Aneurism of arch; much atheroma beyond.	Left lung collapsed; left pleura contained some pints of pus.	Right, surface very granular; both fibrous; weight, 14 oz.	Uterus contained a fibroid.

APPENDIX A.—*Cases of Atheroma*—continued.

Sex, Age, etc.	Vascular System.	Lungs, Pleuræ.	Kidneys.	Other Organs, History, Remarks, etc.
No. 8, M.	Heart, 37 oz.; left ventricle admitted fist; posterior aortic cusp perforated by an ulcer; arteritis.	Pleuræ adherent in parts.	Healthy.	Patient had had syphilis severely.
No. 9, M., 20, costermonger.	Fusiform aneurism of aortic sinus; inner coat of aorta very atheromatous in parts.	Both pleuræ contained moderate amount of clear fluid; some old adhesions, right apex.	Not examined.	Cicatrix of an old bubo in right groin.
No. 10, M., 56.	Atheroma of aorta and of arteries of lower limbs.	...	Shrunken.	History of syphilis. (See R. Johnston, *Path. Trans.* 1890, vol. xi.)
No. 11, M., 56, painter.	Heart, 10½ oz.; aortic valves converted into two tubercular flaps; much atheroma around.	Some threadlike adhesions at apices; left congested, œdematous.	Left, cystic and fibrous; a few miliary caseous bodies.	A large sloughing abscess of scrotum, extending beneath rectus abdominis; several false urethral passages.
No. 12, M., 55.	Aneurism of ascending aorta, bursting into pericardium; aorta very atheromatous above.	Left, congested; œdematous.	Hard and congested; weight, 10½ oz.	Brought in dead.
No. 13, M., general dealer.	Ecchymoses beneath endocardium; pulmonary arteries very atheromatous.	Bronchi, especially of left lung, dilated; upper lobes fibrous; visceral pleuræ semi-cartilaginous, thick.	Weight, 11 oz.; congested, ecchymoses on surface.	Left testis converted into fibrous mass; left epididymis seat of caseous substance.
No. 14, M., 55, clerk.	Several small hæmorrhages in pons; one small cyst in funiculus cuneata; cerebral arteries atheromatous.	Numerous patches of thick pleuræ at apices; left lung compressed by fluid in pleura, in part carnified; no tubercle.	Granular, cystic.	Many miliary fibrous deposits on surface of spleen, none within: history of rheumatic gout.
No. 15, M., about 65.	Large hæmorrhage in left ventricle; aorta, cerebral arteries, etc., atheromatous; heart, 1 lb.; hypertrophied.	...	Right, ½ oz.; left, 6 oz. Right, congenitally undeveloped; left, cystic, fibrous. Urine, 1 per cent. albumin.	Seized with right hemiplegia 14 days before death.

APPENDIX A.—*Cases of Atheroma*—continued.

Sex, Age, etc.	Vascular System.	Lungs, Pleuræ.	Kidneys.	Other Organs, History, Remarks, etc.
No. 16, M., 44, musician.	Two aortic cusps calcified, third fringed with soft growth; cerebral arteries atheromatous.	Pleuræ adherent generally; lungs airless and congested at bases.	Congested, tough, capsules adherent.	(See S. B. H. Reports, vol. xxviii. for history.)
No. 17, M., about 40, collector.	Extensive laceration of brain by hæmorrhage; cerebral arteries very atheromatous; aorta also atheromatous.	...	Small and granular.	Died shortly after admission.
No. 18, M., 25.	Thoracic aorta atheromatous; pulmonary arteries dilated; pericardium adherent.	Right lung coated with thick layers of flaky lymph; left pleura held much fluid.	Large, and very tough and congested.	A large amount of tubercle dotted over peritoneum; tubercular testes.
No. 19, M., 36.	Some atheroma at the commencement of the aorta.	Several vomicæ in left lung; surrounding tissues solid, small white granules scattered over rest of lung; large vomicæ in right lung.	Large and pale, capsules peeled well; pyramids red, well defined; cortex about normal. Urine very albuminous during life.	...
No. 20, M., 54, groom.	Three or four ulcers in ascending aorta; transverse arch very atheromatous.	Pleuræ adherent at apices; large vomica, right lung; fibroid thickening around.	Mottled, shrunken, cystic.	Mucous hæmorrhages from nose and mouth; anasarca; liver fatty.
No. 21, M., 37.	Heart, 22 oz.; dilated and left chambers hypertrophied; aorta atheromatous.	Right lung, two or three cavities in lower lobe; left lung consolidated at base, fibrous tissue thickened; numerous softish adhesions.	12 oz., granular; urine very albuminous during life.	Liver capsule thickened; discrete, glistening; white granules in Sylvian fissure and over pia mater.

APPENDIX A.—*Cases of Atheroma*—continued.

Sex, Age, etc.	Vascular System.	Lungs, Pleuræ.	Kidneys.	Other Organs, History, Remarks, etc.
No. 22, M., 28, clerk.	Thoracic aorta atheromatous throughout; heart healthy.	Many small vomicæ with puckering at left apex; pleuræ much thickened in parts; no tubercle bacilli found in sputa.	Weight, 1 lb. 2 oz.; amyloid; capsules adherent; finely granular surface.	Lower two-thirds of small intestine, and the large intestine dotted over with ulcers, whence pus could be expressed; amyloid reaction to m. m.
No. 23, M., 24, watchfinisher.	Aorta atheromatous; heart healthy.	Firm pleural adhesions; both lungs contained vomicæ with increased fibrous tissue in parts.	Weight, 19 oz.; cortex pale; pyramids red.	Many suppurating ulcers over Peyer's patches.
No. 24, M., 53, policeman.	Aorta atheromatous; heart healthy.	Several vomicæ in both apices; masses of tubercle elsewhere, with adjacent fibrous changes; thready pleural adhesions.	Weight, 6½ oz.; granular.	Many intestinal ulcers; several pints of ascitic fluid in abdominal cavity.
No. 25, M., 55, joiner.	Heart, 14 oz.; pericardium adherent to surrounding organs; serous surface covered with lymph; aorta atheromatous.	Pleural cavities obliterated; scattered miliary tubercles throughout both lungs; cavity, size of a hen's egg at left apex.	Weight, 11 oz.; yellow miliary bodies in substance; capsules stripped readily.	Many intestinal ulcers; bronchial glands enlarged.
No. 26, M., 21, barber.	Some hypertrophy of left ventricle; aorta atheromatous.	...	Capsules somewhat adherent; tough.	Appendix vermiformis had sloughed; purulent fluid in abdominal cavity.
No. 27, M., 11, scholar.	Aorta for an inch above valve atheromatous.	...	Congestive mottling.	The loose end of a sloughed appendix was the seat of an abscess.
No. 28, F.	Some patches of atheroma in ascending aorta; heart healthy; left brachial, subclavian, common iliac veins occluded by firmly adherent clots.	Fluid in both pleuræ; also firm adhesions at apices.	Weight, 8 oz.; granular.	Abscess cavity in the integument above the pubes; anasarca.

APPENDIX A.—*Cases of Atheroma*—continued.

Sex, Age, etc.	Vascular System.	Lungs, Pleuræ.	Kidneys.	Other Organs, History, Remarks, etc.
No. 29, F., 36.	Fringes of soft blood-stained, vegetation on mitral; aortic valve also affected; aorta atheromatous.	...	Capsules thickened; granular, congested.	An abscess cavity at the back of right ovary, shut off from peritoneum.
No. 30, F., 36, barmaid.	Adherent pericardium; aorta atheromatous; right jugular and innominate veins occluded by clots during life.	The upper lobes of both lungs dull red, solid, and firm; recent pleurisy at each apex.	Capsules adherent; surface granular; urine albuminous.	Liver capsules thickened; history of rheumatism, 12 years ago; anasarca general for two weeks before death.
No. 31, F., 43.	Warty growths on mitral valves, opening annular; thrombi in uterine veins.	Right pleura distended with fluid; a patch of intense congestion at base.	Weight ½ lb.: many cysts; urine albuminous.	Fibroid of uterus; anasarca; history of rheumatism.
No. 32, M., 14, machine-boy.	Fibrous growths on pulmonary and aortic valves; chambers dilated and hypertrophied.	Left pleura universally adherent; lungs œdematous and congested.	Irregular congestion.	No history of acute rheumatism; suffered from rheumatic pains; family history cardiac.
No. 33, M., 35.	Aortic mitral curtain seat of ulcer, ½ in. diameter, covered with soft vegetation on ventricular aspect.	A few friable adhesions in both pleuræ; left, lower lobe solid, Temp. 104° before death.	Congested.	Acute rheumatism, four attacks; left hemiplegia 14 years ago for 10 weeks; no emboli observed.
No. 34, F., 52.	Two small ulcers on ventricular aspect of mitral, which was "buttonhole" in shape and calcified.	...	Capsules adherent; surface pitted; cortex thin.	History of acute rheumatism 30 years ago; thighs brawny; fingers with nluar trend; anasarca, twelve months.
No. 35, F., 30, servant.	Heart, 6 oz.; third aortic cusp congenitally undeveloped; some atheroma of aorta; pericardial effusion considerable.	Both pleuræ contained much serum; lungs carnified in parts.	Weight, 7 oz.; tough; pyramids dark blue; cortex thin. Urine seldom albuminous.	Family history of heart and dropsy; facial palsy 12 months ago.

APPENDIX A.—*Cases of Atheroma*—continued.

Sex, Age, etc.	Vascular System.	Lungs, Pleuræ.	Kidneys.	Other Organs, History, Remarks, etc.
No. 36, M., 23, carter.	Heart, 30 oz.; pericardium adherent; mitral and aortic valves thickened.	Many fibrous adhesions to pleuræ.	Not examined.	History of three attacks of rheumatism.
No. 37, M., 34, gardener.	Small rough vegetations on free edge of mitral; granulations dotted over pia mater.	...	Not examined.	History of rheumatic pains in joints; basal ganglia soft.
No. 38, M., 16, errand-boy.	Heart, 17 oz.; adherent and thickened pericardium; tricuspid, mitral, and aortic valves roughened; two last with ulcers.	Pleuræ contained about 3 pints of serum; lungs collapsed at bases, œdematous.	Weight, 7 oz.; shrunken, mottled; urine very albuminous, 70 oz. daily.	Two years ago had stone removed from urethra; pericarditis subsequently; pains in joints without swelling; temperature high.
No. 39.	Heart, 1 lb. 2 oz.; some atheroma of mitral valve and of aorta.	Lungs emphysematous; mucous membrane of colon pigmented and mammilated.	Many ecchymoses; some shrinkage.	Liver, 4 lb. 2 oz.: several cysts in substance filled with bile.
No. 40, F., 33.	Heart, 18 oz.; mitral valve thickened, contracted, and aortic valve fringed with vegetations; no ulcers.	Lungs shrunken and collapsed at bases; old adhesions.	A little cloudy swelling of cortex; two infarcts in right kidney.	Gall-stones impacted in cystic and common ducts; liver ducts dilated and filled with bile; acute rheumatism 12 years ago.
No. 41, M.	Heart, 28 oz.; extensive calcareous changes at both mitral and aortic orifices.	Some effusion into both pleuræ; lungs congested.	Large, hard, dark, 16 oz.; urine, non-albuminous.	Liver nutmeggy; no history of rheumatism nor syphilis; anasarca.
No. 42, M., 32, retired soldier.	Aortic valve converted into a calcareous ring with a central slit-like opening.	Both pleuræ contained fluid; some emphysema.	Intense congestion; cortex thin.	Anasarca 2 years; no history of rheumatism.
No. 43, M., 67, tutor.	Aorta and pulmonary artery very atheromatous; mitral thickened.	Firm adhesions over both lungs, which were emphysematous and œdematous.	Small, congested, granular.	Ill 2 years with bronchitis and asthma.

APPENDIX A.—*Cases of Atheroma*—continued.

Sex, Age, etc.	Vascular System.	Lungs, Pleuræ.	Kidneys.	Other Organs, History, Remarks, etc.
No. 44, M., 62, labourer.	Heart, 20 oz.; mitral and aortic valves thickened and puckered; atheroma of aorta.	Each pleura contained about 1 pint of serum; some old adhesions, some œdema of lungs; no bronchial dilatation.	Weight, 1 lb.; capsules thickened; cystic granular; surface pale.	Anasarca, diarrhœa, anæmia, 15 months; no hæmorrhages.
No. 45, M., 5½.	Aortic valve incompetent through shortening of cusps, and silting up of sinuses (see Plate I. Fig. 8).	Congested.	Tough and congested.	Illness began with fit, 9 months ago; his limbs were swollen and painful at intervals.
No. 46, F., 18, servant.	Aorta just above the valve covered with patches of atheroma.	...	...	Severely burnt 10 days before death.
No. 47, M., 41, servant.	Heart, 20 oz.; dilatation and hypertrophy of left ventricle, valves healthy; pericardial fluid, 5 oz.; renal arteries patulous.	Pleuræ contained 25 oz. of clear fluid; apices of lungs adherent and puckered; bases collapsed.	Weight, 13 oz.; capsules adherent; substance dark, flexible; papillæ shortened; urine very albuminous, scanty.	Had delirium tremens and dropsy two years ago.
No. 48, F., 63.	Advanced atheroma of basal cerebral arteries.	(See Joffroy, App. B.)	...	Peripheral neuritis with right hemiplegia, and softening of left inner capsule.
No. 49, F., 17, ironer.	Heart cavities dilated, muscle pale; streaks of atheroma above aortic valve.	Right lung covered with flaky lymph and solid, in colour greyish yellow; left lung œdematous.	Large, bases of pyramids very congested, elsewhere pale; urine albuminous.	Ill with typhoid symptoms, diarrhœa and lung mischief, with high temperature two weeks before death; no intestinal ulcers.
No. 50, F., 24, none.	Heart dilated; numerous patches of atheroma at the commencement of aorta.	Left pleura filled by a globular mass of tissue firmly adherent to walls; lymphadenoma; left lung pushed downwards.	Large, congested, tough.	Pleuritic effusion on left side 12 years ago; in delicate health subsequently.

APPENDIX A.—*Cases of Atheroma*—continued.

Sex, Age, etc.	Vascular System.	Lungs, Pleuræ.	Kidneys.	Other Organs, History, Remarks, etc.
No. 51, F., 58, matron.	Mitral valve almost occluded by two soft conical growths; the myocardium was soft and friable; aorta atheromatous.	Both lungs dotted over with petechiæ; no adhesions; very œdematous and congested at bases; no infarcts found.	Cortex very thin; capsule adherent and thick; granular, cysts; urine held blood.	Admitted in a semi-conscious state, pulse high tension, limbs œdematous; illness began 5 weeks before admission with diarrhœa; spleen contained many small abscesses; a small abscess was also found just to the outside of the head of the left internal capsule (size of a nut).
No. 52, F., 2½.	Some streaks of atheroma just above aortic valve.	Patches of bronchopneumonia in both lungs.	Very congested; urine very albuminous.	Diphtheritic laryngitis; tracheotomy.

APPENDIX B.

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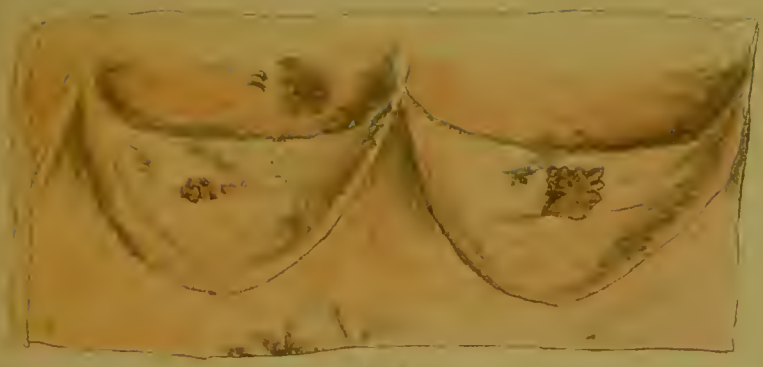

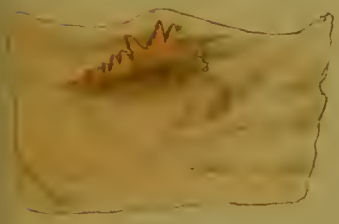

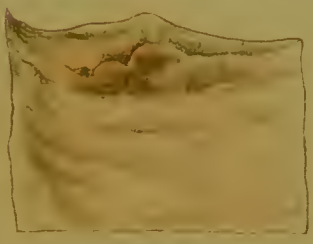

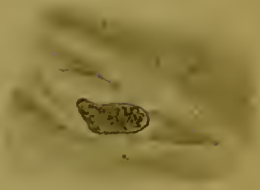

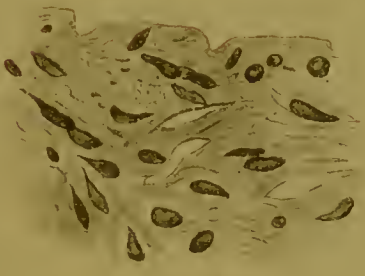

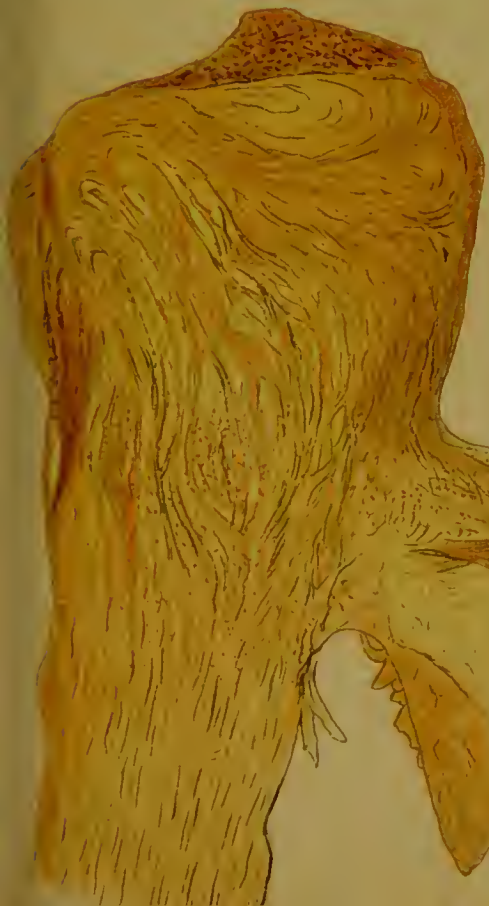

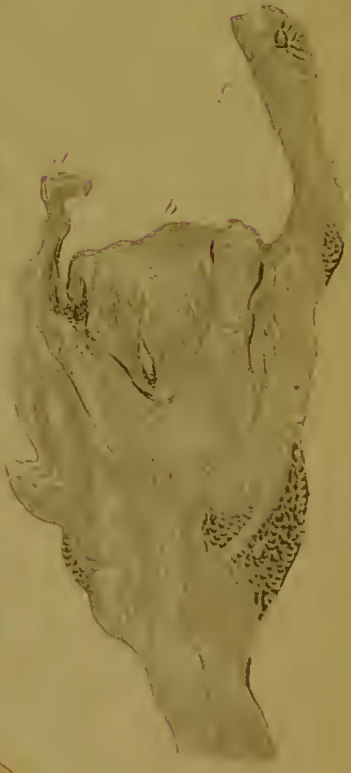

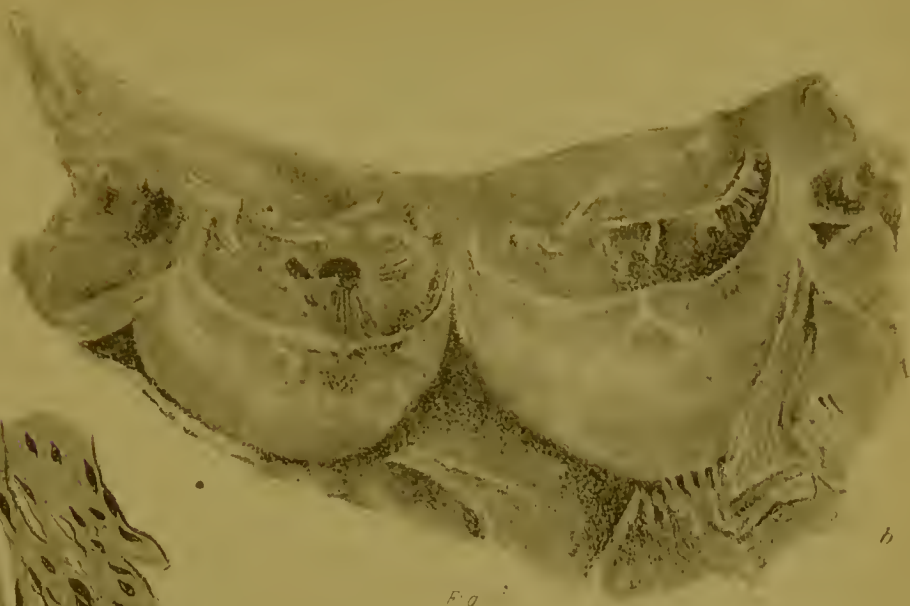

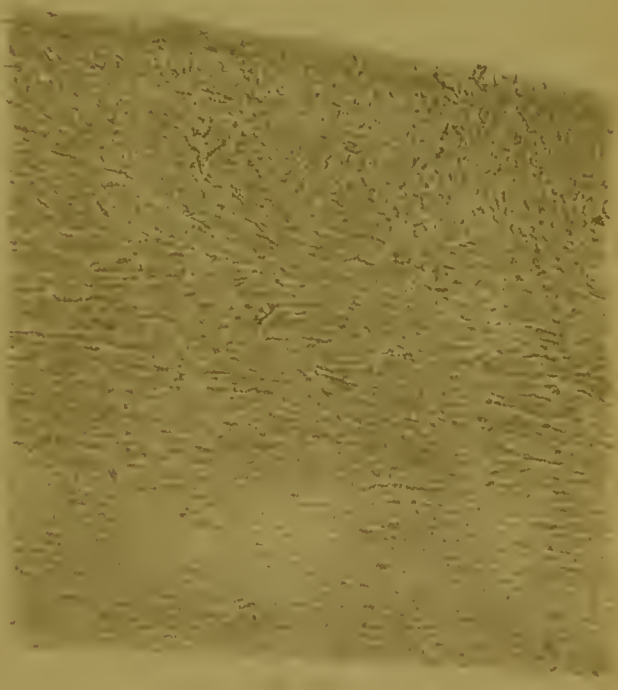

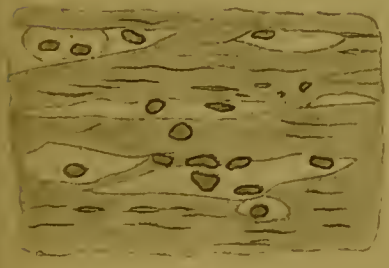

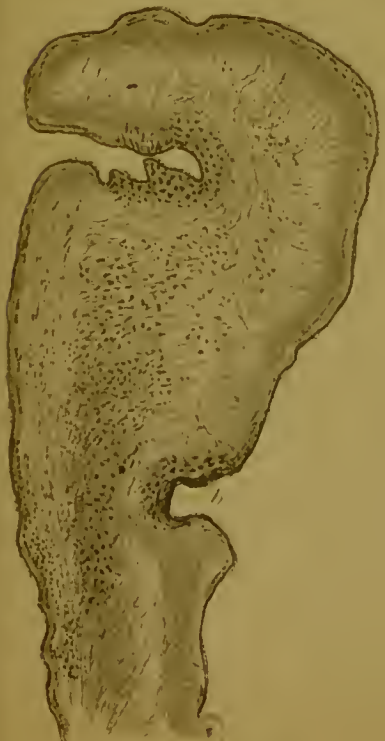

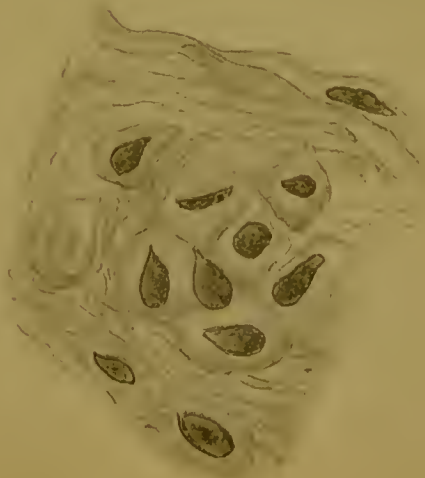

(13)

With the writer's Compliments

II

ATHEROMA.

By W. AINSLIE HOLLIS, M.D. (Cantab.), F.R.C.P.

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ATHEROMA.

(II.)

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(Plate XVIII.)

The Topographical Distribution of Aortic Atheroma and its Clinical Significance.

The frequency with which atheroma attacks aortic ostium as a delicate elevated tracery has been alluded to elsewhere[1] I propose in the following pages to give the results of some further observations on the earlier phases of linear atheroma, with special regard to its topographical distribution along the aorta. For this purpose it will be convenient to consider the artery as divisible into sections. The first of these extends from the ridge forming the uppermost limit of the Valsalvan sinuses to the orifice of the innominate artery,[2] the second includes the remainder of the arch, whilst the third section comprises the rest of the artery.

The circumference of the aortic ostium, along the ridge of the Valsalvan sinuses above mentioned, is divided by the orifices of the coronary arteries into two unequal arcs; that including the attachments of the right posterior flap being as a rule somewhat the longer of the two.[3] The shorter and, for our present purpose, the more important arc, passes through the point of joint insertion of the free edges of the anterior and the left posterior aortic flaps. It also includes that portion of the intima whence springs the band of supplementary fibres which assist in forming the floor of the aortic arch. These fibres have been fully described in a former article.[4] As they have not been mentioned elsewhere to my knowledge, and as they undoubtedly strengthen the aortic walls at the commencement of the artery, just where additional strength is presumably necessary, I feel justified in bringing them again before the

[1] *Journ. Path. and Bacteriol.*, Edin. and London, vol. iii. p. 9.

[2] Atheroma of the sinuses themselves has been already discussed.

[3] The positions of the coronary orifices in relation to the point of joint attachment of the free edges of the anterior and left posterior aortic flaps vary considerably in different subjects. They are, however, mostly as above described.

[4] *Loc. cit.*, pp. 5, 6.

notice of histologists. In the present instance the chief interest consists in their relationship to the linear growth of atheroma along the floor of the aortic arch.

At the commencement of the arch the earliest indications of atheroma are usually met with in the intima, immediately above the shorter of the two arcs, into which the circumference of the aortic ostium may be divided. In young subjects, and possibly in all, who have succumbed to a rapidly fatal disease, the preference of atheroma, if it exists, for certain sites is usually demonstrable. In the more chronic forms of the disease this peculiarity is frequently masked by secondary deposits elsewhere. Even in the latter case, however, the pathologist can often infer the locale of an early outbreak of the disease by the position of an ulcer, or from the presence of a calcified plaque amidst plashes, it may be, of linear atheroma (Plate XVIII. Fig. 6).

To a superficial observer there are few, if any, points of resemblance in the designs traced on the aorta by atheroma. If, however, we compare a series of specimens of aortic ostia, attacked by acute linear atheroma, we can scarcely fail to note one similarity in all the cases, and that is the shape of the atheromatous streaks or lines. These streaks, which are well shown in the two illustrations of thoracic aortæ (Plate XVIII. Figs. 7, 8), are found occasionally throughout the arterial system, and associated with a great variety of diseases. They have also a peculiarity in common, no matter what their situation,—a peculiarity which I find did not escape the observation of the late Dr. Moxon,[1]—and that is, the majority lie with their long diameters parallel to the direction of the blood stream. At the aortic ostium linear atheroma not unfrequently assumes the form of whorls, rings, and sinuous lines; in the descending thoracic aorta, however, and in the lower abdominal region, it is usually to be seen in its simplest forms, as dots, or as narrow straight elevated streaks, about a tenth of an inch in breadth, and of a variable length, some measuring an inch or more. I shall, therefore, begin this account of the topographical distribution of linear atheroma by describing what may be seen when it affects the descending aorta.

The fixed position of the descending thoracic aorta along the spine, its directness, its tubular shape, and its freedom from large branches, together make it the most suitable and interesting vessel to study in the present inquiry. For it is here that we may assume the blood to move onwards in an unchecked "viscous flow," if this motion occurs anywhere in the aortic system.[2] It is here, then, that we may expect to observe the deposition of aortic atheroma under the simplest physical conditions; and, needless to add, under those most favourable to the present investigations. Two cases, recently in the Sussex

[1] "Atheroma forms lines lengthwise to the vessel's course."—Moxon, 1871.

[2] We may, at all events, assume that the blood flows viscously through this vessel, when the circulation is sluggish by failure of the cardiac propulsive power.

County Hospital, are typical examples of linear or streaky atheroma in this region, and they will serve as illustrative texts upon which to append the following remarks. That similar cases are seldom described in post-mortem records is no conclusive proof of their pathological rarity, since the descending aorta is generally left unopened at these examinations. In neither of these autopsies did the condition of the cardiac valves and aortic ostium suggest the probability of extensive atheroma of the descending aorta. The illustrations (Plate XVIII. Figs. 7, 8) are from photographs of the aortæ in question, taken from absolutely untouched negatives.

The first illustration (Fig. 7) represents the aorta of a man who died with symptoms of "rheumatism," associated with hyperpyrexia. The history of the case is given elsewhere,[1] and it is therefore unnecessary to recapitulate. The peculiarity of the aorta consisted in its apparent freedom from disease, until the descending part of the arch was reached, when the intima became flecked with streaks of atheroma, like those above described. At first, that is at the head of the descending aorta, the streaks were distributed generally over the intima. Even here, however, the streaks mainly had their long diameters either parallel to the general direction of the blood stream, or with a marked trend thereto. This peculiarity of disposition is in accordance with the behaviour of atheroma in other parts. When the level of the second pair of intercostal arteries was reached, although many streaks still flecked the intima on either side of their orifices, yet along the dorsal aspect of the vessel, in the intima between the intercostals, the lines of atheroma were more closely crowded than elsewhere. At a still lower level, this concentration of the disease to the site above mentioned was very evident, few if any streaks passing beyond the lines uniting the openings of the right and the left intercostal arteries respectively. Unfortunately, we had not an opportunity of examining the artery beyond the diaphragm, and the topographical description of the diseased vessel must end here. Coincidently with the above peculiar disposition of *acute* atheroma,[2] the whole endothelium over the affected site was extremely friable and readily detachable from the outer coats of the intima, especially over the elevated streaks. Many of these presented rough, eroded surfaces. The inmost layers of the artery at these spots were seen under the microscope to be "frayed out," as it were, and crowded with "nuclear bodies," or vagrant leucocytes, few of which appeared in the deeper layers of the intima or media. There were, however, some swarms of highly-stained nuclear bodies scattered through the loose areolar tissue immediately surrounding the vessel.

[1] Appendix A, No. 66, p. 379.

[2] I think the history of the case justifies this appellation. The condition of the arterial intima tallied fairly well in its general details with the description of acute arteritis given by Rokitansky (Bibliography).

In the other specimen of linear atheroma of the descending aorta,[1] from a case of uræmia (Plate XVIII. Fig. 8), the streaks were few in number throughout the first two-thirds of the arch. It was not until the descending aorta was reached that the disease attained its full development. From this point downwards the inner membrane of the artery was furrowed with numerous short, beaded ridges. Especially was this the case on that strip of intima between the orifices of the intercostal arteries, which, we may remember, proved to be peculiarly susceptible to the attacks of the disease in the former instance. The atheroma was not, however, limited so strictly to this region, as it apparently was in the more acute attack of hyperpyrexia. Commencing at the left-hand corner of the figure, and passing obliquely downwards towards one of the lower intercostals is a light-coloured band, which represents a broad elevated streak of atheroma. It also represents with considerable accuracy a line joining the termination of the floor of the arch and the dorsal aspect of the thoracic aorta, that is, two sites much affected by atheroma in its early stages. The surface of each atheromatous streak was smooth and rounded, and the intima was everywhere firmly adherent, in marked contrast to the other specimen. A section of one of the atheromatous streaks was stained and otherwise prepared for microscopic examination, in a manner as far as possible identical with that employed in the other case. It was then found that the second specimen differed in many important details from the other section, which I have above described. First, a few scattered swarms of nuclear bodies alone had invaded the endothelium at rare intervals, leaving wide reaches of untouched membrane, and they presented an appearance very different from the more general invasion of the endothelium observable in the former example. Very different, too, was the behaviour of the individual nuclear bodies in the two subjects. The specimen we are now considering was riddled, as far outwards as the middle coats with the minute canals, or "burrows" as I prefer to regard them, associated with the dissemination of nuclear bodies throughout the elastic layers of the aortic walls. Each burrow, as a rule, contained one, rarely more, of these deeply stained, pip-shaped bodies. In some cases these bodies seemed to be encapsuled among the fibres of the walls. Others from their faint colour, larger size, and more granular texture, I judged to be undergoing a process of dissolution, such as I described in my previous paper. In the case of hyperpyrexia, it will be remembered, none of these nuclear bodies seemed to penetrate outwards beyond the innermost layers of the intima which were torn and frayed out by the number and the violence of the invaders. Few, if any, were in that case encapsuled, but of those which had penetrated most deeply, many were probably undergoing dissolution.

There is in the histories of several of the cases recorded in the

[1] Appendix, Case No. 59, p. 377.

appended table indirect evidence pointing to the occasional formation of an atheromatous streak within a few days of death. For instance, in the case of a healthy child of 4 years of age, who died 4 days after severe burns, the aorta was streaked with atheroma (Plate XVIII. Fig. 1). In the former paper two or three cases were cited, in which the historical testimony favoured the view that the aortic disease commenced within 10 days of death. More recent evidence on this subject, however, makes it probable that atheromatous tracery may be produced upon a healthy intima within a week. Now let us consider in what way the rapid production of atheroma under certain conditions can tell upon its distribution along the aorta. If we assume, for example, that many streaks of atheroma visible in the aorta of the man, who died of hyperpyrexia, were the growth of a week or less, and neither their aspect nor the history of the case is opposed to this view, we tacitly admit that the arterial mischief was in active progress when the patient was lying supine and helpless in bed; when his dilated heart strove vainly to compensate by rapidity of contraction for the gradual failure of its propulsive powers. Now, if foreign particles of a higher specific gravity than plasma were carried along the aorta by a sluggish blood stream, whilst a patient was lying on his back in bed, they would tend to occupy the lowest strata of the liquid plasma. The location of linear atheroma along the dorsal aspect of the thoracic aorta tallies well with this interpretation of its causation by such foreign particles. We have, however, a still more cogent argument in favour of the hypothesis that, in both the cases I have described above, this arterial disease was due to the introduction of heavy foreign particles into the blood.

Leucocytes, as is well known, are specifically lighter than blood plasma. During their life, however, the want of density does not apparently inconvenience these minute bodies in their progress through the vessels. Nevertheless, this physical relationship between leucocytes and blood plasma must be always present in the living body, always ready to make its influence felt when the time and the place are favourable to that end. There is constantly a tendency, in accordance with the law of gravity, for the blood to differentiate itself into horizontal layers, the heavier particles sinking to the lower strata, and the lighter floating upon the top. During health, when the organs of our bodies are functionally active and vigorous, the operation of this law is unnoticeable. It is, however, otherwise, if through the failure of the heart's contractile powers the blood flows sluggishly within the great nutrient vessel. Then we may expect specific differences of weight among the contents of the aorta to show themselves the more readily, as the circulation slows. When a patient has been lying for some days or weeks upon his back in bed, as in the two cases I have just recorded, we should be justified in assuming, if any change took place in its constitution, that a hyperleucocytosis existed in the upper or

ventral layers of the aortic blood, and that in the dorsal or lower strata there would necessarily be, during the last days of life, a hypoleucocytosis. Now what did the *sectio cadaveris* teach us in regard to this conjecture? Why, that it was quite wide of the mark. All the pathological evidence at our disposal showed, as plainly as such evidence can, that the contrary condition existed in the blood of the aorta at the time of death. That in the first case, especially, the lowermost layer of the blood must have then been swarming with leucocytes; leucocytes which for some set purpose, if such creatures can have purposive actions, had, despite their specific lightness, forced their way through the blood plasma to the dorsal aspect of the vessel. I know of only one explanation of this phenomenon, but that is happily a simple one. The leucocytes visible in the thin sections I have described, as adherent to the walls, or as passing into the layers of aortic intima, were phagocytes, which, after a heavy meal, strove, as is their wont, to free the blood from the contamination of themselves and their ingesta by the shortest possible route.[1] The above facts all tend to confirm the view that the presence of linear atheroma, along the dorsal aspect of the descending aorta, is due to the admixture of specifically heavy foreign particles with the blood.

As regards atheroma of the first section of the aorta, that immediately above the valve, we have here to deal with a tube which is structurally more complex than the one we have just been considering. Owing, also, to the nearness of the heart, its contents are doubtless subjected to greater jerks and jars, to more violent waves and eddies than those which affect the blood elsewhere. Under these physical conditions we cannot expect linear atheroma, if the blood current in any way participates in its formation, here to assume the comparatively simple aspect that it does in the descending aorta. As a matter of fact we find, as I have already stated, that the lines or streaks of incipient atheroma are frequently twisted and otherwise distorted at the commencement of the arch. The loops, whorls, and rings, so commonly seen in this situation, are comparatively rare in the straight descending artery (cf. Plate XVIII. Figs. 5 and 6). There is, however, one topographical peculiarity, affecting both the straight and the sinuous lines in the former position. The disease has a tendency to spread along the floor of the arch, much in the same way, apparently, as it spreads along the dorsal aspect of the thoracic aorta. Not only is this the case, but it frequently happens that other streaks situated around the ostium, yet away from the floor, have a distinct trend on either side towards that part; that is to say, every such streak would form, if produced, a more or less acute angle,

[1] This subject has already been somewhat fully considered (*loc. cit.*, vol. iii. p. 15). It is probably outside the present inquiry to speculate how leucocytes can sink in the blood, in opposition to their gravity, and I do not feel inclined to act as nature's apologist in this matter. I may suggest, however, that by closely adhering to the endothelium, leucocytes possibly move without difficulty in many directions along a vessel's walls.

with a line passing longitudinally along the centre of the floor. I have measured, in different cases of well-marked trending, the angles so formed on either side of an imaginary base line along the floor of the arch. I shall not reproduce these measurements here, as they were necessarily approximate only, and until they can be more accurately determined it is needless to publish them. I may state, however, as a general result of several observations on seven different subjects, in five of them streaks near the left attachment of the anterior cusp that formed angles considerably over 45 degrees (but less than 90 degrees) with the line in question, while others adjacent to the right attachment of the right posterior cusp formed, when produced in the manner suggested, with one exception only, angles very much smaller than 45 degrees. It will seem, then, that in these cases there is, first, apparently a tendency for streaks of atheroma to pass along the floor of the aorta, with their long diameters in the general direction of the blood stream. Secondly, that streaks on either side of the floor, yet not actually upon it, frequently have a trend in the same direction.[1] In chronic forms of atheroma these peculiarities of its growth along the first section of the arch are usually masked, and sometimes obliterated.[2]

As regards the remainder of the arch the chief interest centres in the terminal portion, just above the descending thoracic aorta. At its union with the latter the arch appears to twist somewhat upon itself. Just below the orifice of the left subclavian artery, and upon the opposite side of the arch, is the real termination of the floor. This spot, where the intima is somewhat uneven owing to the presence of bundles of supplementary fibres, is frequently the seat of atheroma in its early stages (Plate XVIII. Fig. 2). The openings of the large vessels are also often affected, although in these cases atheroma spreads mostly along the sides of the branch vessel, and not at first along the aortic walls. There is usually at the head of the descending thoracic aorta a slight dilatation anteriorly. This is often splashed with atheroma; indeed, the arrangement of linear atheroma at this part of the aorta is very irregular, and there is apparently an absence of that preference for particular sites so noticeable in other divisions of the artery.

The following conclusions are the outcome of the observations discussed in the foregoing pages:—

1. There are satisfactory clinical, pathological, and histological evidences that atheromatous streaks may be formed during the last few days of life by the passage of leucocytes more or less deeply into the lining membranes of a previously healthy aorta.

[1] As the imaginary base line along the centre of the floor of the aortic arch is difficult to determine with accuracy, it has been found advantageous in practice to use as base lines, first, a line passing through the uppermost limits of the attachments of the anterior cusp; secondly, a similar line through those of the right posterior cusp. These base lines are far more satisfactory than the other, and show the amount of trend of an atheromatous streak in this locality with facility.

[2] I have elsewhere considered how these changes arise (*loc. cit.*, p. 10).

2. The presence of linear atheroma, specially along the dorsal aspect of the descending aorta, in subjects who have spent the last few days of life upon their back in bed, suggests that the leucocytes, which are specifically lighter than blood plasma, were attracted to that side of the artery in opposition to the law of gravitation.

3. In these cases—(1) the previous introduction of heavy foreign particles into the blood; (2) the gradual subsidence of these particles; (3) their subsequent ingestion by phagocytes; and (4) their rapid removal by these bodies from the circulation, together offer a simple explanation of the pathological phenomena.

4. The favourite situation of linear atheroma of the aortic arch is the floor or lesser curvature.[1]

5. The atheromatous streaks usually point with their long diameters in the direction of the blood stream.

Sectional Calcification of the Aorta, from an Anatomico-Pathological Standpoint.

In the former article on atheroma a considerable amount of evidence was offered in favour of the hypothesis that the arterial disease was always preceded by the introduction into the blood of minute foreign particles, injurious to the host. The observations recorded in the earlier pages of the present paper confirm, in an indirect manner, the above proposition as regards linear atheroma, a disease peculiar to childhood, youth, and early middle age. They, however, leave untouched the ætiological relationship of that rare and interesting disease of advanced life, wherein the aorta along a part of its length only is more or less completely calcified. When the area of intima affected in this extreme manner is limited to the abdominal aorta, the remainder of the vessel being relatively free from the disease, as happened to two patients formerly under my care,[2] it would seem probable that some supplementary factor of importance in the causation of atheroma had been omitted from consideration. It was to ascertain to what extent this peculiar disposition of calcareous atheroma affected the validity of what had heretofore seemed a good working hypothesis, that I undertook the following inquiry.

I have, unfortunately, been unable to collect more than six cases of extreme calcareous atheroma of the aorta, notes of which are given in the appended table. Four of the cases have come under my personal observation, and of the remainder, one is the hospital specimen above mentioned (No. 4); the other consists of a case recorded by my

[1] The situation of acute atheroma along the floor of the arch by preference may account for the rarity with which this disease of the intima terminates in aneurism, which usually springs from the convex side (Bibliogr. *Oppolzer, Gee*). It is very doubtful whether atheroma is often the cause of aneurism (Thorburn).

[2] Case No. 5, vol. iii. p. 23, and Case No. 53, p. 376.

colleague, Mr. T. J. Verrall (No. 55), and photographed by Dr. A. J. Richardson. Of the whole number two only are examples of sectional calcification of the abdominal aorta (Nos. 5 and 53). We must not, however, conclude that this disease is consequently exceptionally rare, but rather that, from one reason or another, it has not attracted the attention of pathologists, and the conservative energy of curators of hospital museums.[1]

If we separate the alimentary canal into two hypothetical divisions at the pylorus, we shall obtain two tracts of mucous membrane, differing largely in function. The upper portion consists mainly of a tube for the reception and preparation of the crude materials from which our bodies derive their health and strength. On the other hand, within the intestinal canal is situated the most important absorbent system we possess, for here the prepared food is absorbed, and to some extent even incorporated within us. This arrangement of the alimentary system lessens the risks we all run of direct blood contamination, through the introduction of injurious foreign particles with the chyle. For owing to the distance the pylorus is from the mouth the chance of aërial infection is diminished, and, in submitting the food to the processes of mastication and stomachic digestion, it is mainly rendered aseptic, and many living germs introduced along with it are probably destroyed, that is to say, so long as the organs are functionally sound, and the epithelial lining intact.[2] The nutrient vessels of the alimentary canal throughout the greater part of its length are, as we may remember, somewhat peculiar. They are noted for the large number of arterial anastomoses between the branches of the chief nutrient vessels. This is specially the case as regards the lower section of the canal; and a reason for the arrangement here is probably an obvious one. It must undoubtedly be important that the nutrition of such a functionally active absorbent system should be always efficient, even under occasionally adverse conditions. Yet the intestines deal largely with crude food material as it passes the pylorus, and render this stuff both chemically and physiologically capable of healthful assimilation within our bodies. In dealing with this material, I imagine, there must be an occasional, I shall not call it a frequent, risk of the temporary blockage of some of the terminal arterioles, by the accidental introduction of crude particles into the

[1] As far as I am able to ascertain, the specimen in the Museum of the Sussex County Hospital is unique; at all events, it is doubtful whether the metropolis can furnish a similar specimen. Unfortunately, as is so often the case with ancient museum specimens, the clinical history is deficient. Guy's Hospital, I believe, possesses one of the finest collections of diseased aortæ in England; but even here some of the older specimens are deficient in this respect.

[2] If the researches of Kaufmann are correct, different micro-organisms behave differently in the presence of free hydrochloric acid; generally speaking, those which split up the carbohydrates, and those causing lactic acid fermentation, are most resistent. On the other hand, those that split up nitrogenous material are the most susceptible.

blood stream. Now the system of arterial anastomosis mentioned above will reduce the inconvenience, not to say danger, of an arterial block to the nutrition of the mucous membrane surrounding it. The circulation in such a patch of membrane will, despite the thrombus, be carried on much as usual, until phagocytes have removed the impediment. It is conceivable that a small artery may be obstructed in various ways, for instance by fat globules, or by the introduction even, through osmosis, of some free acid or other reagent having the property of chemically coagulating the blood, and not necessarily by an invasion of living microbes. The risk of accidental blockage from one of the above causes must be incurred, if at all, by the mesenteric arterioles, and I think that this explanation of the necessity for arterial anastomoses in this circulatory district is a plausible one. It may not be the only reason for the peculiar vascular arrangement we here find, possibly it is only one of many.

When, however, we turn our attention to the upper division of the mucous tract, that above the pylorus, the anastomotic character of the arterial circulation cannot be accounted for in the above manner, for although the mucous membrane of the stomach may have some absorptive power, the pharynx and œsophagus can scarcely have functions of this kind. Yet it is especially with this part of the alimentary tract that I am about to deal. There is, moreover, a further vascular peculiarity as regards the lower part of the œsophagus and the cardiac end of the stomach, one set of their anastomotic vessels arises as small short branches directly from the aorta. The arteries supplying the remainder of the tube, *e.g.* the ascending pharyngeal, the superior thyroid, and the inferior thyroid, anastomose freely with each other, and thereby with the upper œsophageal branches of the aorta, although their relations with the largest artery of the body are not so close, it may be, as are those of others lower down. We have, at all events, one district of mucous membrane in very near circulatory relationship with the aorta, namely, that of the lower gullet and stomach cardia.

Although leucocytes are endowed with certain spontaneous locomotory powers, it is improbable that they can make headway against the blood current even in the capillaries, where the flow is sluggish. In the aorta and large arteries, where the flow is rapid and often turbulent, the majority are swept onward with the blood. It is probable, too, that the greater number of bacteria, when introduced into the vessels, are also carried along by the blood, although they may be capable of independent locomotion. Intermittent and desultory movements in particles suspended within a liquid stream will not, I take it, greatly affect their translation by the stream through space. When, however, an artery is blocked at its distal end, and the circulation through it has ceased, there exists no impediment to the free movements of any particles capable of locomotion in the contained

blood so long as the latter remains fluid[1] on the proximal side of the thrombus between it and the next arterial orifice. We may expect, under these conditions, that both leucocytes and bacteria may occasionally pass backwards through the stagnant blood to the nearest vascular opening, to be again swept onwards to the capillaries by the blood stream.

Arterial anastomosis favours the blocking of an artery at the distal end, when a thrombosis takes place within an anastomotic district; for, of two inosculating vessels, one, usually the smaller, must necessarily be obstructed at its distal end, unless the whole vessel is occluded by the clot, an occasional accident. In the former, and I imagine the more usual case, an arterial *cul-de-sac*, blocked at one end by a clot and containing fluid blood, will be the result. This vascular recess, if the thrombus was due to infection, might speedily become the breeding-place of pathogenic microbes, and the happy hunting-ground of leucocytes. Hence, engorged phagocytes and bacterial swarms might readily find access to the general circulation.

Let us now return to the six cases of aortic calcification, which were alluded to at the beginning of this article (Nos. 4, 5, 20, 53, 54, and 55 of Table). The selection of these cases has mainly depended upon the following circumstances. Of three (viz. Nos. 20, 53, and 54) I still possess portions of the aortæ. One specimen is in the Sussex County Hospital Museum, as above stated; and of one other I have the photograph, as before mentioned. One alone of six cases rests its claims to inclusion with them upon a historical description. As, however, the description was written by myself shortly after the autopsy, or upwards of a quarter of a century before this paper, and many years before I had turned my attention to the investigation of atheroma, personal equation cannot, I imagine, have prejudicially affected it. As regards the disposition of the atheroma, the disease affected the arch, the thoracic, and the abdominal aorta in a third of the cases respectively. Of the two in which the arch was attacked, one had kidney fibrosis and hæmorrhagic ulcers of the hard palate, and the other had a somewhat doubtful history of a malignant gastric ulcer. The calcification of the thoracic aorta was associated with malignant hepatic disease in one case, with malignant disease of the œsophagus in the second. Finally, there was a definite history of extensive and chronic ulceration of the stomach in both the cases of calcification of the abdominal aorta. The ulcers had invaded the cardiac extremity of the organ in each instance. We have then in these six cases of extreme calcareous changes in the aortic coats, a history of extensive ulceration of the upper part of the alimentary canal in five, and of malignant disease of the liver in one. Again, there is a clear history

[1] It is well known that stagnant blood may remain fluid within a living vessel for a long period; the experiments of Lister with the jugular vein of a horse proved even more than this (Bibliogr.).

of malignancy, in the sense usually ascribed to this word, in three patients; and in two others the disease of the stomach was probably of this nature. In patient (No. 20) with fibroid disease of the kidneys there was no evidence whatever pointing to a malignant taint. Malignancy seems, as far as my experience avails me, to play an important, although by no means essential, part in the causation of aortic calcification.[1]

It is, however, to the association of aortic calcification with one or more ulcers in the upper section of the mucous tract that I wish to direct attention at the present time. In all the six cases, save one, there is a history of chronic ulceration—mostly of a hæmorrhagic type—in some part of the alimentary canal above the pylorus. In the excepted case, one of malignant hepatic disease, the history is so imperfect, and the possibility of the malignant growth being of a secondary nature so considerable, that I shall omit it from consideration at present. There remain five cases of chronic hæmorrhagic ulcers of the mucosa. As the interest of these cases centres mainly in the sectional calcification of the abdominal aorta, I shall commence with a consideration of the two cases (Nos. 5 and 53). In each of these subjects the ulceration was confined to the cardiac end of the stomach. The first was undoubtedly carcinomatous. The whole of the cardia was occupied by a large ragged ulcer, about 4 in. across, and nearly circular in shape. The walls of the stomach outside the ulcers were firmly adherent to the adjacent viscera. Many secondary growths, circular in shape and with depressed centres, were visible beneath the peritoneal coat of the liver, others were found in the lungs, vascular, yellowish tumours, in some instances with gritty or caseous centres. Under the microscope, the growth had the histological characters of carcinoma. The abdominal aorta was converted into a rigid calcareous tube for about 4 in. above the bifurcation. There was atheroma elsewhere, at the aortic ostium and at the commencement of the arch, but the disease was comparatively slight. The thoracic aorta was dilated. In the second case, on the posterior surface, and close to the cardiac orifice at the commencement of the lesser curvature, were two ulcers, with pigmented surfaces and somewhat thickened submucous bases. The larger had an area of $1\frac{1}{2}$ in. by $\frac{1}{2}$ in. A tortuous vessel passed close to the ulcers. The intestines contained much blood clot. There had been repeated hæmorrhages from the bowel during life. There were no secondary growths in any viscus. In this case, as in the preceding one, atheroma had attacked

[1] A search through the Metropolitan Museums for cases in any way resembling those above alluded to has been for the most part fruitless. In Guy's Museum the catalogue refers to a specimen (1462), "a portion of aorta with spots of earthy deposit, from a man who died of cancer," but the specimen had apparently been removed. In the University College Museum (3047), there is a specimen of pyloric ulceration, associated with which was a small aortic aneurism with calcareous walls.

the cardiac valves somewhat, and a few patches of the disease were seen on the thoracic aorta, which was also dilated. It was not, however, until the diaphragm was passed that the full extent of the vascular mischief was obvious. The aorta had apparently been converted into an inelastic calcareous tube. In these two cases, then, we have two remarkable coincidences, namely, extensive ulceration of the mucous membrane of the cardia, associated with those rare changes in the coats of abdominal aorta, which I have named *sectional calcification.* The coincidences are rendered the more interesting when we remember the close vascular connection there is between the cardiac end of the stomach and the aorta, through the arterial anastomoses of the coronary artery of the stomach with four or five aortic œsophageal branches. Any large and deep excavations in the stomach walls, situated as these ulcers were at the cardiac orifice, would necessarily interfere with the anastomotic vessels, blocking some and destroying others. It is conceivable, owing to its shortness and its direct relationship with each affected district, namely, the cardia on the one hand and the aorta on the other, that one or more of the chief œsophageal branches might be occluded by a clot, and a direct backward communication established with the abdominal aorta in the manner I have described. If the deposition of calcareous matter within an arterial wall is brought about by the agency of leucocytes, by a method analogous to that described elsewhere,[1] the sudden incursion of a horde of half-poisoned phagocytes into the aorta at the spot mentioned would probably lead to a sectional calcification of the aortic walls, similar to that actually found in Cases 5 and 53, unless it produced a still more serious, because a more acute, condition of the main nutrient vessel of our bodies and its contents. Why sectional calcification of the abdominal aorta should be, under these circumstances, an unusual accompaniment of gastric ulcers depends doubtless on a variety of causes, some of which I shall now recapitulate.

An important factor in the etiology of sectional calcification of the aorta, if the œsophageal arteries enact the part I have assigned to them, will be the position of the stomachal ulcer.[2] It is evident that unless the ulcer is so situated at the cardiac orifice as to interfere with the flow of blood through one of the main œsophageal branches of the aorta, the sequence of pathological events, suggested in the case of abdominal aortic calcification, cannot take place. Conversely we might

[1] *Loc. cit.*, pp. 11, 12.

[2] Drs. Perry and Shaw, in their careful analysis of the specimens of malignant disease of the stomach in Guy's Hospital Museum, found the pylorus involved in 70 per cent. of the cases. The lesser curvature rarely escaped. The greater frequency with which the pylorus is attacked in these cases may help to account for the rarity of the associated aortic disease. Of perforating gastric ulcers, Mr. Barling says: "A large majority of these ulcers occur on the posterior surface and lesser curvature. A few occupy the region of the pylorus, and a still smaller number involve the anterior surface of the stomach."—"Ingleby Lectures," 1895, iii.

expect sectional calcification of the thoracic aorta, as distinguished from that of the abdomen, to be associated, if at all, with ulcers of the alimentary canal, situated at a higher point than the stomach. I have unfortunately been unable to obtain more than one example of extreme atheroma of the descending thoracic aorta with a sufficient clinical history. It is Mr. Verrall's case of a carcinomatous ulcer of the œsophagus, perforating the trachea (No. 55). There is no mention of the exact position of the ulcer in this case, but from the fact that it perforated the trachea it must have been situated several inches above the stomach. Now in this case the descending thoracic aorta was the vessel most seriously affected, and the orifice of the uppermost œsophageal artery was apparently embedded in a thick atheromatous plaque, which plainly showed that the aortic disease extended so high in the thorax (Plate XVIII. Fig. 9). The inferior thyroid artery anastomoses with this aortic branch. Such evidence as this single case affords favours the assumption that sectional calcification of the descending aorta depends largely upon the anatomical arrangement of the nutrient arteries of the œsophagus and stomach. Although I have been unable to obtain any other case of sectional calcification of the thoracic aorta, with a satisfactory clinical history, I have met with a case of fungoid aortic growths, which will throw some light upon the subject we are considering.

The small branches given off by aortæ just below the arch are irregular in their origin. There is in a certain percentage of subjects a small œsophageal branch, which arises close to the termination of the floor of the arch, about half an inch below, and on the opposite side to the opening of the left subclavian artery. This branch, when it exists, is considerably above, and not in a line with, the highest right intercostal artery. It is also much smaller than this vessel. I imagine that the former becomes not seldom blocked and obliterated. At all events, I have met with a minute depression on the intima at the spot where the uppermost œsophageal branch usually comes off, in subjects where this artery was apparently absent.

On 11th February 1893 an old man was admitted in an emaciated and exhausted condition to the Sussex County Hospital, where he died two days afterwards. There was a history of progressive emaciation, associated with dysphagia for two years previously. On opening the œsophagus a patch of ulceration, about an inch in length, and reaching almost around the tube, was found on a level with the bifurcation of the bronchi. A few fungoid-looking growths were attached to the wall of the œsophagus. There was very little thickening. A slit-like opening, about half an inch long, was visible between the base of the ulcer and the trachea. The opening was just over the right bronchus. The arch of the aorta and the apex of the left lung were adherent to the growth. Several cavities filled with pus, and with smooth walls, were found in the upper lobes of lungs; the largest at the right apex. On cutting into the aorta, the lower wall of the arch, which was adherent to the growth, presented a fungoid-looking vegetation, soft, and readily peeling from the intima, and about the size of a threepenny-bit. The adventitia at the base of

this growth was apparently healthy. There were two or three smaller patches, presenting a similar appearance, lower down. The heart was healthy.[1] On examining the aortic growth and the subjacent patch under the microscope, the former consisted apparently of a fibrous stroma, with a loose irregular network, within the meshes of which were many "nuclear bodies," or vagrant phagocytes. The patch was formed of the aortic intima, and possibly the inner layer of the media, which had been invaded by leucocytes, and, as usual, frayed out and damaged by them.

We have here an example of a soft fleshy growth upon a patch of atheromatous tissue such as is commonly found upon the cardiac valves, and rarely elsewhere. Now the chief interest in this case arises from the situation of the aortic growth, and its relations to the œsophageal ulcer, which, by the way, was on a squamous epithelial carcinoma. The site of the aortic patch was adjacent to the orifice of the uppermost œsophageal artery, the chief nutrient vessel, with the inferior thyroid of that part of the mucous membrane destroyed by the ulcer. Unfortunately the condition of the artery was not observed at the autopsy, and I am unable to state whether it was blocked by clot or not. However that may be, it is scarcely credible that a vessel connecting the ulcerated œsophageal surface with the diseased aortic intima would come off scathless. Again, the extremely local character of the aortic mischief pointed to some equally local cause at work producing it. If a plug was formed in the upper œsophageal branch of the aorta, a line of communication between the mucous ulcer and the aorta might at any moment be established through the stagnant blood, in the way I have previously explained. That the aortic intima immediately surrounding the vessel's orifice became diseased under these circumstances would not be surprising, for this case tends to show, like those I have before alluded to, that ulcers of the gullet may, through the arrangement of the œsophageal nutrient vessels, determine the position of an atheromatous aortic plaque.[2]

Other factors in the causation of sectional aortic calcification besides the *position* of a chronic mucous ulcer are doubtless its size and depth, the shape and condition of its walls, and so forth. It will thus be seen that the exceptional rarity of sectional calcification in the abdominal portion of the vessel is not surprising, especially when we consider the frequency with which an examination of the aorta is omitted at autopsies.

Of the three remaining cases of aortic calcification, not yet referred to, the arch was the part chiefly affected in two. In only one of these subjects, a patient of mine, was the history quite satisfactory. This

[1] I am indebted to Mr. Mallam, a former house physician, for the notes of the above autopsy (No. 69).

[2] In the museum at Guy's Hospital there is a specimen (No. 1501[24]), described as a "small blood clot, the size of a filbert, adherent to a slightly atheromatous patch on the aorta, just above the pillars of the diaphragm. Patient, 66, admitted with epithelioma of the œsophagus in a very emaciated condition." This case doubtless resembled the one I have above quoted in many particulars.

case was one of extensive atheroma, along with numerous ulcers in various parts of the arch and at the commencement of the thoracic aorta. The patient, a stableman, suffered from renal inadequacy,[1] and, towards the end of life, from frequent hæmorrhages from the buccal and intestinal mucous membranes. That from the mouth was found to come mainly from an ulcer situated on the roof, at the line of junction of the hard and soft palates. The nutrition of the mucous membrane of the pharynx and mouth, although largely carried on by anastomotic vessels, is not so closely connected with the aorta as is that of the lower gullet. Any infective material absorbed by an ulcer within this region would have to pass the usual circulatory round, in order to arrive at the aortic ostium. The length of the systemic series of vessels in such cases would be comparatively a short one to traverse, and it would be one that was remote from the chief blood purifiers, namely, the spleen and the kidneys. Under these conditions a larger percentage of the poisonous matter might pass the aortic ostium in a given time than would be the case if the foreign matter had found its way into the blood current at some more distant point. This, however, is only a question of degree, and not of kind. We cannot expect to find any special local peculiarities, differentiating atheroma of the aortic ostium, originating in chronic buccal ulceration, from that due to an iliac ulcer, for instance.

Finally, it may be contended that the above cases, although they show an association to exist between ulcers of the alimentary canal and atheroma, do not admit the interpretation I put upon them; and that the atheroma may have been the cause of the ulcer in many if not all the examples I have adduced. The old theory that gastric ulcers mostly originate "in affections of the vessels connected with the diseased area, especially embolism or degenerative change of the arteries," may be true to an extent. It is not, however, the whole truth. Degenerative changes in the arteries supplying mucous membrane, adjacent to an ulcerating patch, would probably lead to an enlargement of the area of the latter. Dr. S. Fenwick, who has studied the subject carefully, asserts that where the arteries are healthy in gastric ulcers, the veins of the mucous membrane are generally dilated and thickened. If we admit the occurrence of gastric ulcers, without the presence of diseased arteries, we undoubtedly greatly weaken the arguments of those who would make arterial atheroma the cause of all such ulcers. The cases narrated above show that a relationship exists between the position of chronic mucous ulcers of the upper part of the alimentary tract and the location of aortic atheroma. The only interpretation of the

[1] Dr. W. H. Dickinson called attention to the occurrence of ulceration of the bowel with granular kidney in the Croonian Lectures for 1876. More recently he has collected twenty-two examples. In two cases the stomach was ulcerated as well as the bowel. The most marked character of the ulcers was their association with hæmorrhage.—*Proc. Roy. Med.-Chir. Soc.*, vol. vi. p. 36.

phenomena which satisfies both the anatomical and the pathological requirements of the case would seem to be the one that I have above given.

DESCRIPTION OF PLATE XVIII.

The plate contains figures of aortic ostia affected with atheroma. Three of them may be considered to represent fairly typical examples of the acute disease, whilst the others are examples of a more chronic form.

FIG. 1.—Atheroma of aorta after a burn, 4 days previously. Girl, 4½ years. Case 68.

FIG. 2.—Commencing atheromatous ulcer at the termination of the floor of the arch of aorta, after a burn. Boy, 3½ years. Case 67. (*a*) The ulcer.

FIG. 3.—Atheroma in a case of tubercle. Case 58.

FIG. 4.—Atheroma in a case of typhoid fever. Case 63.

FIG. 5.—Atheroma of the aorta from a case (No. 60) of granular kidneys, with symptoms of uræmia before death.

FIG. 6.—Extreme atheroma of the aortic ostium, from a case of malignant gastric ulcer. Case 54. (*a*) Atheromatous ulcer at the commencement of the floor of the arch.

FIG. 7.—Linear atheroma of the descending thoracic aorta, from a case of "rheumatic" hyperpyrexia. Case 66. From an untouched negative photograph.

FIG. 8.—Linear atheroma of the descending aorta, from a case (No. 59) of uræmia. From an untouched negative photograph. Figs 7 and 8 about half natural size.

FIG. 9.—Extensive calcareous atheroma of the thoracic aorta, in a case of carcinoma of the gullet. Case 55. From a photograph by Dr. A. J. Richardson.

APPENDIX.

Table of Cases of Atheroma, showing various Diseases with which the chief Organs were concurrently affected. Continued from p. 23.

Sex, Age, etc.	Vascular System.	Lungs, Pleuræ.	Kidneys, etc.	Other Organs, History, Remarks, etc.
No. 53, M., 65, retired.	Heart, 26 oz.; tricuspid and mitral valves thickened; pulmonary ostium dilated; aortic valve atheromatous; some patchy atheroma over thoracic aorta; abdominal aorta almost completely calcified.	Right lung much collapsed; left, fibrous tissue thick; cut ends of vessels stood out rigid on section.	Capsules adherent; shrunken; renal arteries tortuous and atheromatous.	Close to the cardiac orifice of stomach, at posterior aspect of lesser curvature; two ulcers with pigmented thickened bases; large tortuous vessel passed near them.
No. 54, M., 50–60.	Aorta extremely atheromatous with much ulceration. Fig. 6.	Unrecorded.	Unrecorded.	A large (malignant?) ulcer of the stomach.
No. 55, M., middle-aged.	Descending thoracic aorta very atheromatous. Fig. 9.	Apex of left lung gangrenous. Mr. Verrall's case.[1]	Unrecorded.	Carcinomatous ulcer of the œsophagus, perforating trachea.
No. 56, M., 24, cabman.	Heart dilated; valves healthy; aorta atheromatous at commencement.	Pleural cavities contained fluid; right lung contained tubercles; left, collapsed and fibrous in parts; bronchioles dilated.	Congested.	Both layers of peritoneum studded over with tubercular granules.
No. 57, F., 13.	Edges of mitral curtain thickened; spots of atheroma on the aorta.	Pleuræ dotted with discrete yellow tubercles; lungs studded with grey miliary tubercles; bronchial glands tuberculous.	Bases of pyramids congested; a few yellow tubercles in cortex.	Pia mater contained many tubercular granules; bad cough 3 months; headache 10 days before admission.
No. 58, F., 23, wardmaid.	Heart, 7½ oz.; pericardium distended with serum; mitral valve atheromatous; also aorta. Fig. 3.	Right pleura adherent; lungs' weight, 44 oz.; cavities at both apices partly filled with reddish grumous fluid; recent tubercle at right base.	Weight, 8½ oz.; cortex plus and pale; no lardaceous changes.	Had suffered from winter coughs since childhood; frequent hæmoptysis; family consumptive.

[1] *Proceedings of the Brighton and Sussex Medico-Chirurgical Society*, September 6, 1894.

APPENDIX.—*Cases of Atheroma*—continued.

Sex, Age, etc.	Vascular System.	Lungs, Pleuræ.	Kidneys, etc.	Other Organs, History, Remarks, etc.
No. 59, M., 28, gardener.	Heart, 13 oz.; left ventricle hypertrophied; valves healthy; thoracic aorta atheromatous. Fig. 8.	Lungs intensely congested.	Weight, 5½ oz.; red and tough; cortex very thin; no cysts; urine, ¼ albumen, scanty.	Symptoms of kidney mischief for 3 months before admission; semi-conscious, and with total suppression of urine 5 days before death.
No. 60, M., 32, fruiterer.	Heart, 20 oz.; cavities much dilated; aorta atheromatous. Fig. 5.	Some apical adhesions; lungs œdematous and congested; Fibroid changes at both apices, with scars on pleural surface.	Weight, 13 oz.; capsules thick and adherent; granular in parts.	Moribund when admitted; history of excessive beer drinking.
No. 61., F., 22, domestic.	Left ventricle hypertrophied; tough sprouting growth on mitral valve.	Pleural adhesions at apices; lungs congested.	Capsules adherent in parts; cortex mottled; weight, 19½ oz.	For history, see end of this table.
No. 62, M., 19, undertaker.	Heart, 23 oz.; right cavities dilated; mitral orifice contracted; flaps fringed with atheromatous sprouts; aortic valve also atheromatous.	Right pleura generally adherent; right lung œdematous; left, collapsed.	Right, 7½ oz.; left, 4½ oz.; capsules adherent; urine very albuminous.	Within the inner capsule of right cerebral hemisphere was a cavity the size of a pea, no softening. For history see the end of this table.
No. 63, F., 18, housemaid.	A decolorised clot, size of a marble, attached firmly to apex of left ventricle; aorta atheromatous. Fig. 4.	Unrecorded.	Cloudy swelling of cortex; urine albuminous.	Admitted 16 days before death with symptoms of enteric fever.
No. 64, M., 8.	A considerable patch of atheroma on mitral valve; aortic valve reddened.	Numerous embolic infarcts of a dark red colour, size of peas, in lungs.	Cortex congested and swollen; urine albuminous.	Diphtheritic exudation in larynx, etc.; cellulitis of right side of neck; necrotic slough on upper lip; in hospital 2 or 3 weeks.

APPENDIX.—*Cases of Atheroma*—continued.

Sex, Age, etc.	Vascular System.	Lungs, Pleuræ.	Kidneys, etc.	Other Organs, History, Remarks, etc.
No. 65, M., 11.	Mitral valve œdematous; several streaks of atheroma at commencement of the aorta.	Some congestive œdema of both bases; a tough valvular flap of membrane hanging freely in trachea from mucous membrane of larynx about 2 in. downwards; tracheotomy wound below.	Capsules stripped; intense congestion of pyramids; cortex pale.	Admitted on fourth day of illness, 24 hours before death, with paroxysms of dyspnœa; stridor; diphtheritic exudation on left tonsil; 5 c.c. Ruffer's antitoxin on fourth day of illness; tracheotomy attempted before death.
No. 66, M., 29, furniture remover.	Heart, 11 oz.; some dilatation of cavities; valves fairly healthy; thoracic aorta beyond arch much streaked with atheroma. Fig. 7.	Lungs very œdematous and congested at bases; pleuræ normal.	Weight, 13 oz.; capsules stripped; cortex thick and congested; urine, a trace of albumen.	Skull thick; arachnoid opaque over vault, and cortex congested. For history of this case of hyperpyrexia see at end of this table.
No. 67, M., 3½.	One small patch of atheroma on mitral valve; commencing ulceration of intima at the beginning of thoracic aorta. Fig. 2.	Normal.	Normal.	Died within a week after severe burns over thighs and abdomen; no intestinal ulcers.
No. 68, F., 4½.	Several streaks of atheroma over aorta. Fig. 1. Mitral valve fringed with small vegetations.	Normal.	Normal.	Died 4 days after receiving burns on body, head, and arms; no duodenal ulcers.
No. 69, M., 82, lodging-house keeper.	A soft fungoid growth on intima of aorta, close to the termination of the arch.	Many abscess cavities in upper lobes of both lungs.	Apparently healthy.	Epithelioma of œsophagus; ulcer opened into trachea.
No. 70, M., 69, shoemaker.	"Cat's tongue" lymph on visceral pericardium; several patches of atheroma on descending thoracic aorta.	Recent lymph over both lung surfaces; left lung solid throughout; upper lobe in a state of grey hepatization; lower lobe reddish, breaking down; right lung congested.	Cortex thin; contracted and granular surface; urine contained few chlorides.	Ill 4 days.

History of Case, No. 66.—The patient, whose previous health had always been good, with the exception of influenza 18 months ago, was suddenly attacked with sore throat, and pain, redness, and swelling of the knees, and other joints; for 3 weeks before admission he was confined to bed; on arrival at the hospital he was semi-delirious, with a temperature of 105° F. There was moderate effusion into both knees, a weak, rapid pulse, and some albumen in the urine. The heart's apex was somewhat displaced outwards, and there was a maculated red rash over skin of chest, abdomen, and inner side of arms; in places there were minute pustules. Shortly before death, which took place 2 days after admission, he became wildly delirious, and the temperature rose to 108°·6 F.